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JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

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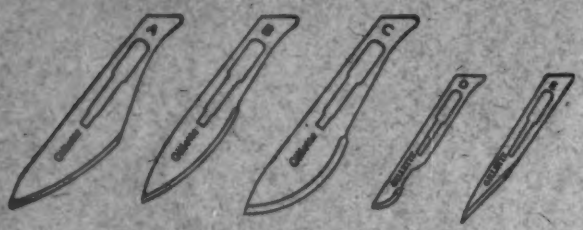

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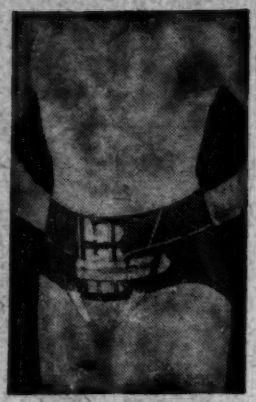

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY FEBRUARY 4 1950

DEATHS FROM INFLUENZA—A STATISTICAL AND LABORATORY INVESTIGATION*

BY

C. H. STUART-HARRIS, M.D., F.R.C.P. ZENA FRANKS, B.Sc.

AND

D. TYRRELL, M.B., Ch.B., M.R.C.P.

(From the Department of Medicine, University of Sheffield)

[WITH PHOTOGRAVURE PLATE]

The reason for this investigation was the correlation, abundantly demonstrated in the past fifteen years, between the height of the recorded deaths from influenza in the great towns of England and Wales and the ability to incriminate by laboratory procedures one or other of the influenza viruses in cases of clinical influenza. When the deaths from influenza in the great towns have exceeded in the aggregate a weekly total of 100, positive evidence of virus infection has been obtained in the laboratory, whereas when the weekly total has not risen above 100 the laboratory search for influenza virus has usually been fruitless (Stuart-Harris, 1947).

It seemed possible that an analysis of the clinical findings in cases recorded by practitioners as deaths from influenza during an epidemic year might disclose points of contrast with similarly recorded deaths in non-epidemic years. In planning the investigation care had to be taken not to influence the decision of the practitioner at the time of death by prior warning, and the records about to be described were obtained by writing to practitioners in urban areas of the Sheffield and East Midlands Region when a certification of a death from influenza had reached the medical officer of health concerned. A post-card was first sent to such practitioners asking if they were willing to supply further clinical details; to those replying in the affirmative a record sheet was sent which could be filled in simply by ringing code numbers. The completed sheets were then transcribed on to punch-cards, and these were analysed by the aid of a Powers machine in the usual way.

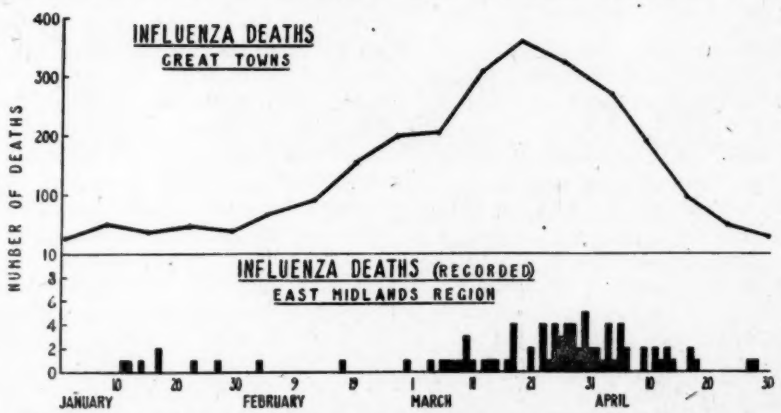

Chart showing the number of deaths from influenza in the East Midlands region in relation to the total weekly figures for England and Wales from January to April, 1949.

The investigation began in September, 1947, and from then until December, 1948, a total of 11 record sheets were obtained from 29 notifications. During this period influenza deaths remained at a very low level and no outbreaks of influenza were encountered. This investigation furnished only a very small sample for comparison with the data obtained during the epidemic period of January to April, 1949, when 192 notifications were received and a total of 85 record sheets were completed; 46 of these were from Sheffield practitioners. The time of occurrence of these deaths from influenza is shown in the Chart in relation to the total weekly figures for England and Wales.

Because of the smallness of the control series no detailed comparison was possible between the practitioners' records in the two series. But the data recorded on the death certificate enabled the age and sex and seasonal distribution and classification of the causes of death in the 29 inter-epidemic cases to be compared with the similar data in the 85 epidemic cases (Tables I and II). Each group was subdivided into four categories according to the immediate cause of death recorded on the death certificate under I (a): (1) cardiac, including the diagnoses of heart failure, myocarditis, and myocardial degeneration; (2) influenza and influenzal pneumonia; (3) pneumonia—including lobar pneumonia, bronchopneumonia, and unspecified varieties; and (4) bronchitis.

It should be noted that the Registrar-General's weekly records of deaths from influenza in the great towns include all cases with mention of influenza anywhere on the death certificate except London. In that town and in all annual figures influenza deaths are considered to be only those in which influenza is reported as the primary cause of death and therefore entered under I (*b*) or I (*c*) on the death certificate (personal communication from Dr. W. P. D. Logan, of the General Register Office). As the weekly

*Based on a communication read to the Pathological Society of Great Britain and Ireland in July, 1949.

TABLE I.—*Age and Sex Distribution*

Age	Jan.–April, 1949 Epidemic					Sept., 1947–Dec., 1948 Inter-epidemic				
	Cardiac	Influenza	Pneumonia	Bronchitis	Total	Cardiac	Influenza	Pneumonia	Bronchitis	Total
0–9 ..	—	—	—	3	3	—	—	—	—	—
10–19	—	—	—	—	—	—	—	—	—	—
20–29	—	—	1	1	2	—	—	—	—	—
30–39	1	—	—	1	2	—	—	1	1	2
40–49	4	3	2	—	9	3	—	2	—	5
50–59	2	—	1	—	3	2	—	2	—	4
60–69	10	5	5	2	22	2	2	3	1	8
70–79	12	11	4	3	30	5	1	1	1	8
80–89	5	5	2	—	12	—	—	1	1	2
90+..	—	2	—	—	2	—	—	—	—	—
All ages	34	26	15	10	85	12	3	10	4	29
Male	15	7	6	5	33	7	1	2	2	12
Female	19	19	9	5	52	5	2	8	2	17

Seasonal Distribution

	Jan.	Feb.	Mar.	Apr.	May–Aug.	Sept.	Oct.	Nov.	Dec.	
1947	—	—	—	—	—	1	1	4	2	Inter-epidemic
1948	4	3	7	—	1	—	2	—	4	Inter-epidemic
1949	7	3	48	27	—					Epidemic

TABLE II.—*Primary and Secondary Causes*

	Immediate Cause of Death I (*a*)							
	85 Epidemic Cases				29 Inter-epidemic Cases			
	Cardiac	Influenza	Pneumonia	Bronchitis	Cardiac	Influenza	Pneumonia	Bronchitis
	34	26	15	10	12	3	10	4
I (*b*) (*c*) Primary:								
Cardiac	8	7	—	—	2	—	—	1
Influenza ..	27	—	15	8	9	—	10	3
Pneumonia ..	4	1	—	1	—	1	—	—
Bronchitis ..	7	2	—	—	2	1	—	—
II Secondary or contributory:								
Cardiac	3	5	2	2	—	1	1	—
Influenza ..	6	—	—	1	3	—	—	1
Chronic bronchitis	1	1	1	1	—	—	2	—

records have chiefly been used in connexion with our own laboratory data, no case was excluded from the present series because of remoteness of influenza as a cause of death.

Table I shows that in both series the majority of the deaths occurred in those aged 60 and over, but that there were no differences between the age distributions in the two series. In both series the sex distributions showed a larger number of females than males, but the excess of females was chiefly in those aged 60 and over, and was only slightly disproportionate in comparison with the sex distribution of the population at these ages. Table II gives a further subdivision of each series which indicates the frequency of the primary and secondary causes of death, again classified into the four main groups of cardiac, influenza, pneumonia, and bronchitis. The frequent occurrence of influenza and other respiratory conditions as primary causes of death where the immediate cause of death was classified under "cardiac" was noted in both series. However, this analysis of the data recorded on the death certificates failed to reveal any obvious differences between the inter-epidemic and the epidemic series of cases.

The circumstances recorded by the practitioners on the record sheets sent to them were examined in detail only in the 85 epidemic cases. It was first noted that the practitioners considered that a local outbreak of influenza existed in 69 instances (81%), and that equal numbers considered this outbreak to be mild and sharp respectively. Because the cases were mostly in old people, the size of the family was small and children resident in the house were few in number in the majority of cases. Indeed, in 46 instances no children were resident in the house at all. Two types of illness had been considered as possible—the one in which the illness was continued from onset to death, and the other in which a complication occurring after an interval had been the cause of death. In 73 cases (85%) the illness was recorded as being continuous from start to finish, and in 9 (10%) it was interrupted. The duration of illness was one to five days in 26 (30%), six to ten days in 35 (41%), and more than ten days in 22 (26%). The fact that only one-third of the illnesses lasted for one to five days was surprising, and indicated that the majority were less acute than had been expected.

Table III analyses the cases according to the character of the principal initial illness and the principal respiratory and cardiovascular complications. The same four major

TABLE III.—*Principal Initial Illness and Principal Complications of 85 Epidemic Cases*

	Immediate Cause of Death				
	Cardiac (34)	Influenza (26)	Pneumonia (15)	Bronchitis (10)	Total (85)
Principal initial illness:					
(*a*) Influenza	30	19	15	8	72
(*b*) Bronchitis	16	11	2	3	32
Respiratory complications:					
(*a*) Bronchitis	16	12	1	7	36
(*b*) Pneumonia—acute ..	6	7	11	1	25
(*c*) Pneumonia—terminal	4	7	3	1	15
(*d*) Pulmonary oedema..	2	2	1	—	5
Cardiovascular complications:					
(*a*) Heart failure—acute	19	10	5	3	37
(*b*) Heart failure—long-standing	12	6	3	2	23
(*c*) Arteriosclerosis ..	9	6	2	1	18

subdivisions were used in the sorting of the cards in an attempt to determine whether or not the entire group was reasonably homogeneous in regard to these characters or whether it included a series of cases with special characteristics. Influenza, either alone or with bronchitis, occurred in 72 cases as the initial illness, and bronchitis, either alone or with influenza, in 32. Of the respiratory complications, pneumonia was mentioned in 40 instances, being of a terminal character in 15. Of the cardiac complications, heart failure, either acute or long-standing, was mentioned in 60 instances. Consideration of the complications in the various groups showed that 26 of the 34 cases in which death occurred immediately from a cardiac cause had bronchitis or pneumonia. Conversely, 16 of the 26 cases of influenza, 8 of the 15 cases of pneumonia, and 5 of the 10 cases of bronchitis had what was described as heart failure. It seemed largely to have been a matter of chance whether a practitioner considered death to have been due to the heart failure of myocardial disease resulting from influenza or pneumonia or, conversely, to influenza or pneumonia in a patient exhibiting signs of heart failure.

The remaining data, such as the state of the previous health and the character of previous chest or heart disease, indicated no sharp difference between the various groups, and suggested merely the existence of previous conditions, such as bronchitis, hypertension, or coronary disease, that might be inferred from the ages of the patients.

In regard to treatment, penicillin had been given in 19 instances and sulphonamides in 54.

Thus the picture which emerged from the analysis of the 85 epidemic cases suggested that the illnesses were not widely divergent in clinical type. Written notes supplied by practitioners in comments which could not be analysed statistically suggested that an elderly subject had developed a pyrexial illness accompanied by signs of bronchitis which

C. H. STUART-HARRIS, ZENA FRANKS, AND D. TYRRELL: DEATHS FROM INFLUENZA

FIG. 1.—Trachea from Case 4. Most of epithelium desquamated and replaced by exudate of leucocytes and fibrin.

FIG. 2.—Trachea from Case 2. More advanced change than Fig. 1. Epithelium replaced by a necrotic slough.

FIG. 3.—Bronchiole from Case 2. Necrosis of entire wall; dark areas of necrotic epithelium are massed cocci.

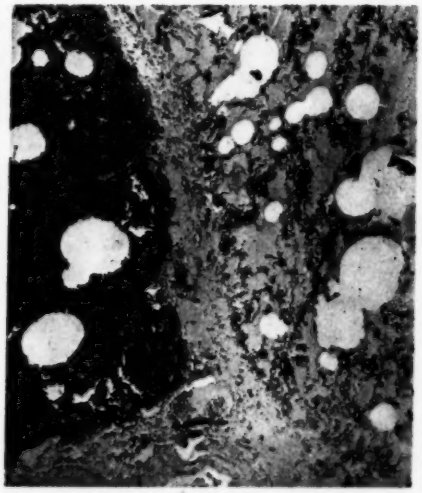

FIG. 4.—Lung from Case 2. Edge of area of haemorrhagic infarction with extensive oedema in rest of lung.

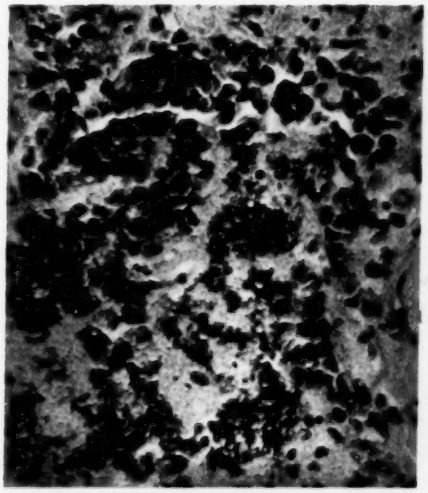

FIG. 5.—High-power view of lung of Case 2. Intense congestion and masses of cocci; little leucocytic reaction.

F. DUDLEY HART AND P. COLLARD: ACUTE IDIOPATHIC PORPHYRIA

FIG. 1.—Right sciatic nerve, showing lymphocytic infiltration with perivascular leucocytes and mononuclear cells.

P. H. BUXTON AND A. WILLCOX: ENDOTHELIOMA OF THE PLEURA

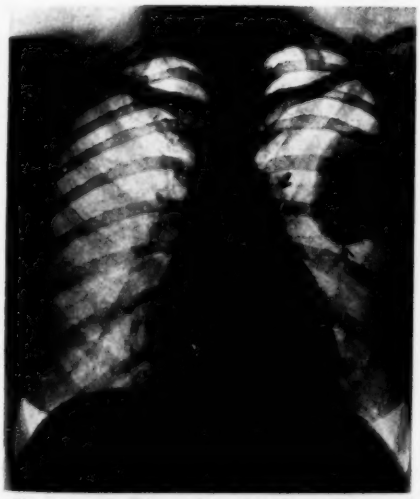

FIG. 1.—Radiograph of chest, December, 1947, showing rounded shadows on the left side.

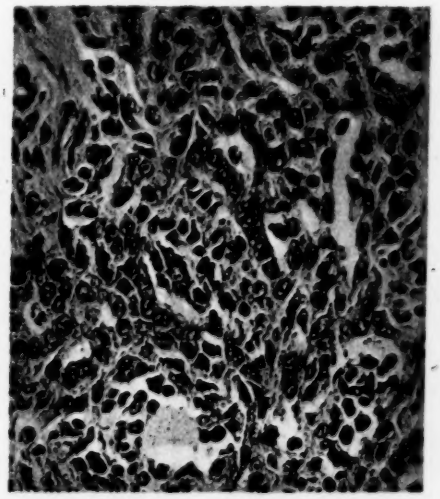

FIG. 2.—Biopsy specimen showing the spindle-shaped cells in whorled arrangements. (× 260.)

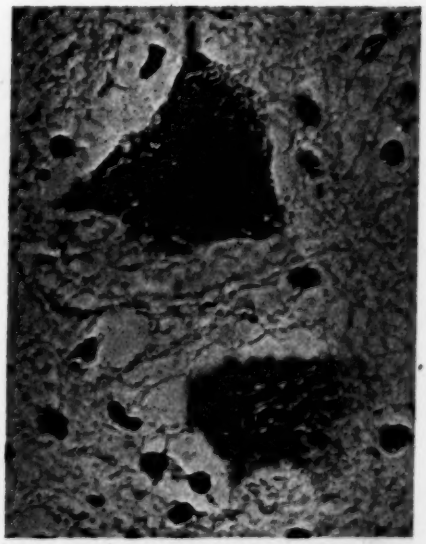

FIG. 2.—Section of lumbar cord showing chromatolysis in anterior horn cells.

J. WALTER: EPITHELIOMA AND PAPILLOMA ARISING ON RECENTLY IRRADIATED SKIN

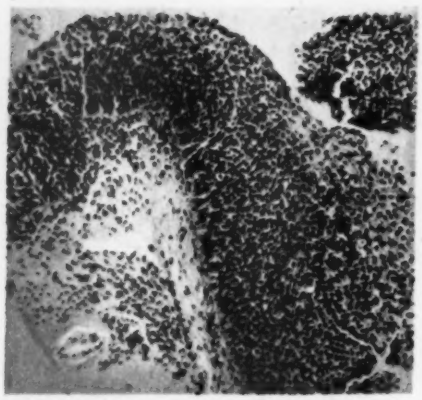

FIG. 1.—Case 1. Original Grade 3 squamous epithelioma of the left vocal cord. (× 80.)

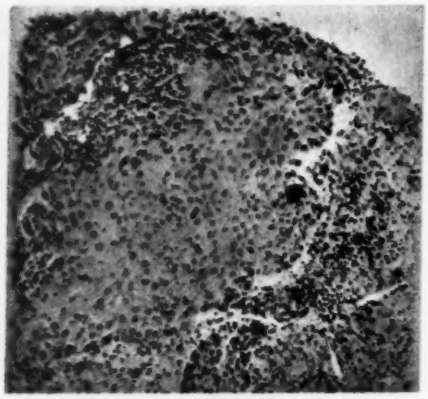

FIG. 3.—Case 2. Original Grade 2 squamous epithelioma. (× 80.)

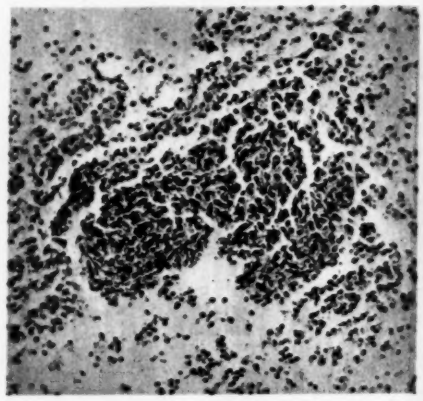

FIG. 5.—Case 3. Original anaplastic squamous carcinoma. (× 80.)

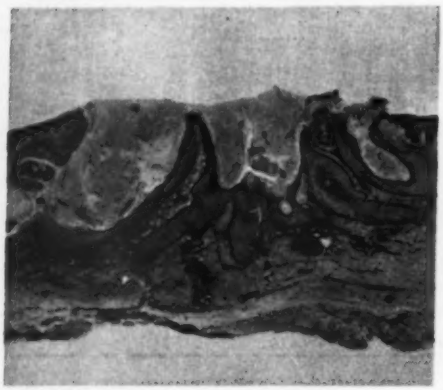

FIG. 2.—Case 1. Simple squamous papilloma of neck after radiotherapy. (× 10.)

FIG. 4.—Case 2. Grade 1 squamous epithelioma after radiotherapy. (× 75.)

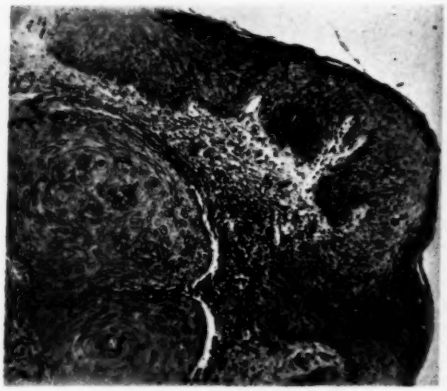

FIG. 6.—Case 3. Grade 1 squamous epithelioma after radiotherapy. (× 50.)

F. I. POWELL: FRACTURE OF THE FIRST RIB

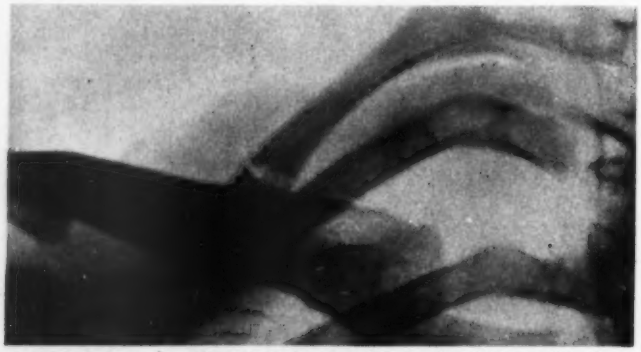

FIG. 1.—Case 1. Complete fissure of first rib with no widening medially.

FIG. 2.—Case 2. "Oblique" fissure of first rib with fissure line widened out medially.

FIG. 3.—Old fracture of first rib with callus formation (buttressing appearance).

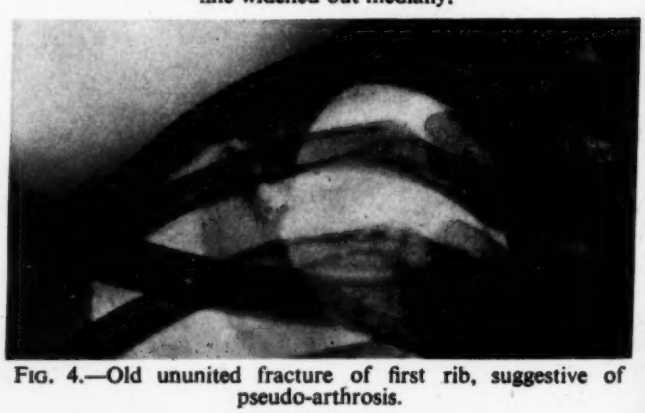

FIG. 4.—Old ununited fracture of first rib, suggestive of pseudo-arthrosis.

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may or may not have improved after one or two days. Sudden increase in illness with severe dyspnoea and cyanosis, signs of consolidation, or diffuse rales then supervened, and death occurred relatively quickly in spite of chemotherapy. From the data it was not possible to obtain any picture of the condition of acute heart failure which was mentioned in 37 of the 85 cases, but it may be the state of low blood pressure with tachycardia and feeble heart sounds which is familiar in many grave infections. Though circulatory in origin, it may be due to a peripheral vascular rather than to a central cardiac failure.

Twenty-two Fatal Illnesses During the 1949 Influenza Epidemic

During the same period of the influenza epidemic in Sheffield there occurred an unexpected opportunity of investigating a number of illnesses which had a fatal outcome in hospital. There were 22 such cases, which occurred between January 28 and April 16, 1949. They formed part of a larger investigation of the relationship between influenza and pneumonia (Stuart-Harris *et al.*, 1950). Seventeen of the cases were examples of acute pneumonia, three were of congestive cardiac failure, and there was one case each of diabetic coma and of cerebral haemorrhage. All but five of these cases were submitted to necropsy, and bacteriological examination of portions of lung were carried out; the sputa from the five on whom post-mortem examinations were not made were examined bacteriologically. Virus tests consisted of amniotic inoculation of 13-day fertile hens' eggs with lung or sputum emulsion to which penicillin and streptomycin had been added in order to suppress bacterial growth.

The distribution of these cases by age and sex (Table IV) gives a somewhat similar pattern to the practitioner series of deaths from influenza, and there was again a predominance of female cases. The pneumonia cases could be subdivided according to the presence or absence of a history of influenza, but no sharp clinical differences existed between the subgroups. The bacteriological results enabled the series to be classified into those cases from which a strain of influenza virus was obtained and those which failed to yield virus either from sputum or from the lung.

TABLE IV.—*Twenty-two Fatal Illnesses*

Age	Pneumonia with a History of Influenza	Pneumonia	Congestive Heart Failure	Other Causes	Total
1	1	—	—	—	1
1–29	—	—	—	—	—
30–39	1	1	—	—	2
40–49	1	1	—	1	3
50–59	1	3	—	—	4
60–69	4	3	2	1	10
70–79	—	1	1	—	2
All ages ..	8	9	3	2	22
Male ..	2	5	1	—	8
Female ..	6	4	2	2	14

The virus-positive cases consisted of eight cases of clinical pneumonia and one case of congestive heart failure (Table V). Five of the patients with pneumonia gave a history of influenza at the onset of illness. A virus with the general properties of influenza virus was recovered from the lung in five instances and from the sputum in four. The strains of virus are still being examined serologically, but so far seven have proved to be influenza virus A on the basis of haemagglutination–inhibition tests. Moreover, they belonged to the same serological subgroup as other influenza A strains recovered during the 1949 epidemic in Britain or sent from the continent of Europe to the World Influenza Centre at Hampstead (personal communication from Dr. C. M. Chu).

TABLE V.—*Virus-positive Cases*

Case No.	Age	Sex	Condition	Duration (Days)	Bacteriology (Lung)
1	46	F	Tracheitis; pneumonia; lung abscesses	5	*Staph. pyogenes*
2	60	F	Tracheitis; pneumonia	7	,, ,,
3*	49	F	Pneumonia; lung abscesses	8	,, ,,
4	36	F	Tracheitis; pneumonia	3	,, ,,
5*	59	F	Clinical pneumonia; no necropsy	5	*Staph. pyogenes* (sputum)
6	63	M	Bronchopneumonia (epilepsy; diabetes)	7	*Staph. pyogenes*
7*	53	F	Clinical pneumonia: no necropsy	11	No culture
8*	69	M	,, ,, ,,	18	Pn. III; strep. haem.
9	66	F	Congestive cardiac failure (hypertension)	7	*Bact. coli*

* Virus recovered from sputum.
Staph. pyogenes = Coagulase-positive staphylococci.

Coagulase-positive staphylococci were found in lung or sputum of six of the virus-positive cases, being present often in enormous numbers in the sputum and as the sole aerobic organism in the lung. These cases were regarded as staphylococcal pneumonia. A Type III pneumococcus and a haemolytic streptococcus were found in the sputum of one virus-positive case, and *Bact. coli* was present in the lung of the case of congestive cardiac failure. The sputum from the ninth virus-positive case was treated with streptomycin and penicillin before cultivation was carried out, and bacteria were not recovered from this specimen.

TABLE VI.—*Virus-negative Cases*

Case No.	Age	Sex	Condition	Duration (Days)	Bacteriology (Lung)
10	65	M	Lobar pneumonia (R.L.L.)	5	Pn. III
11	66	F	Bronchopneumonia	8	,, ,,
12	71	M	,,	3	*H. influenzae*
13	63	F	,,	7	*Proteus*; *Bact. coli*
14*	55	M	,,	4	*Str. viridans*; Staph.
15*	61	M	,,	7	Pn. XIX (sputum); *Staph. pyogenes* (sputum and lung)
16	39	F	Clinical pneumonia; no necropsy	3	*Staph. pyogenes* (sputum)
17	9/12	F	Relapse bronchopneumonia	3	*Staph. pyogenes*
18	52	M	Lobar pneumonia; aortic stenosis	5	,, ,,
19	77	F	Congestive cardiac failure (bronchopneumonia)	2½ mos.	*Bact. coli*
20	68	M	Congestive cardiac failure. No necropsy	1 mo.	Staph. (sputum)
21	68	F	Diabetic coma	5	*Staph. pyogenes*
22	41	F	Cerebral haemorrhage; hypertension	1	,, ,,

* Sputum as well as lung negative in eggs. Staph. = Coagulase-negative staphylococci. *Staph. pyogenes* = Coagulase-positive staphylococci.

The virus-negative group included nine cases of pneumonia, two of congestive heart failure, and two of miscellaneous conditions (Table VI). Two of the patients with pneumonia gave a history of influenza. Two patients (Cases 12 and 19) had been in hospital for one month and six weeks before death, which occurred rather unexpectedly. The original diagnosis was chronic bronchitis and emphysema in Case 12 and hypertensive heart failure in Case 19. Analogous conditions for virus isolation existed in all these cases, as in the virus-positive ones, except that the necropsy was carried out in certain instances without preliminary refrigeration of the body, and the necropsy in Case 12 was not done until 24 hours after death, at room temperature.

Coagulase-positive staphylococci were recovered from the lung in five instances, being present in large numbers in three. Smaller numbers of cocci found in the lung of Cases 21 and 22 may have resulted from an aspiration of faucial secretion during the coma which preceded death. One (Case 16) of the two cases which were not submitted to necropsy had enormous numbers of staphylococci in the sputum, and this case and the two others with heavy growth of cocci from the lung were considered to be cases of staphylococcal pneumonia. Case 18 was complicated by the presence of aortic valve disease and may conceivably have been a case of bacterial endocarditis. The bacteriological findings in the remaining virus-negative cases included Type III pneumococci in the lung in two instances (Cases 10 and 11—husband and wife) and a number of other organisms, including coagulase-negative staphylococci, in the remainder.

It must be remembered that all but one of the cases of pneumonia and of cardiac failure had been heavily treated with penicillin, and in some instances with sulphonamides as well. In five the staphylococci recovered from the lung at necropsy were examined by Dr. J. Colquhoun, of the Royal Sheffield Infirmary and Hospital, for sensitivity to penicillin. Two strains were fully sensitive, but three resisted the action of 1,000, 125, and 32 units of penicillin respectively, and were therefore penicillin-resistant. Ten of the strains of staphylococci recovered from sputum or lung were sent to the Central Public Health Laboratory at Colindale for phage-typing by Dr. R. E. O. Williams. The phage type 52A was identified in five of the strains, all of which were recovered from the cases of pneumonia. The prevalence of this type of staphylococcus may have been peculiar to Sheffield, but it was suggestive of a particular relation to the cases of staphylococcal pneumonia.

Discussion

The conclusions drawn from this series of fatal illnesses were that influenza virus was a frequent invader of the lower respiratory tract in cases of fatal pneumonia during the epidemic. The character of the death in such cases was sometimes that of acute pulmonary oedema, but in others circulatory phenomena, such as low blood pressure, feeble heart sounds, or gallop rhythm, suggested the existence of peripheral vascular or myocardial failure. It is probable that some such phenomena would have been described by practitioners as acute heart failure. The possibility exists that the small series of hospital cases was not unrepresentative of the larger series recorded by practitioners as deaths from influenza.

Fatal staphylococcal pneumonia has in the past chiefly excited attention when occurring in subjects younger than the majority of cases of influenzal pneumonia. It is then recognized because of its association with intense dyspnoea and livid "heliotrope" cyanosis. Unless the recent number of cases in Sheffield was an exceptional occurrence, the combined influenza virus and staphylococcal infection of the lung is not rare or confined to young subjects. It seems to resist current methods of chemotherapy. The post-mortem appearances and histology in such cases are striking, and the cases in the present series (Figs. 1–5, Photogravure Plate) showed the necrosing tracheitis and purple oedematous lung described by Winternitz *et al.* (1920) in the 1918 pandemic and more recently by numerous observers, including Parker *et al.* (1946). But in the 1918 pandemic the characteristic lesions were not associated solely with staphylococci as they have been in all recent outbreaks. The major difference between recent epidemics and the 1918 pandemic is the absence of much involvement of the 20–40 age-group—a fact again borne out by the figures recorded above.

Finally, the present investigation has not fulfilled its purpose, because of the small number of inter-epidemic deaths from influenza yet studied. But the laboratory data recorded above seem to justify the use of the phrase "death from influenza" by practitioners, at any rate during an epidemic of influenza.

Summary

A comparison of a group of 29 recorded deaths from influenza during an inter-epidemic period and 85 deaths from influenza during the 1949 influenza epidemic is described. The age and sex distributions and the immediate, primary, and secondary causes of death were not significantly different in the two series.

Analysis of clinical records of the 85 notified deaths during the epidemic period indicated a close relation between respiratory conditions and cardiovascular complications. No evidence was found that the series included a particular clinical group.

Twenty-two fatal illnesses in hospital during the period of the epidemic in Sheffield were investigated for evidence of influenza virus infection. Nine cases yielded influenza virus from sputum or lung, eight were cases of pneumonia, and one was a case of congestive heart failure.

Staphylococcal pneumonia was an important cause of death among the cases admitted to hospital, and six of ten such cases yielded a strain of influenza virus.

This work would not have been possible without the assistance of the many practitioners who supplied details of patients under their care or without the help of the medical officers of health who advised us of the notifications. We are indebted to various physicians and pathologists who permitted us to obtain specimens from patients and at necropsies. We wish to thank particularly Drs. K. J. G. Milne, E. G. G. Rhind, and C. G. Cook, of the City General Hospital, Dr. C. Gray Imrie, Professor E. J. Wayne, Dr. A. W. D. Leishman, and Dr. L. D. Hermitte, of the United Sheffield Hospitals. Dr. J. L. Edwards not only assisted considerably with the post-mortem specimens from patients at the Royal Hospital, Sheffield, but supplied the sections from which the photomicrographs were prepared. Lieutenant-Colonel S. M. Vine, R.A.M.C., of the Northern Command Laboratory, Catterick, kindly provided us with specimens from one case. Pneumococcus typing on the cultures indicated was performed by Miss M. Pownall, of the Public Health Laboratory, City General Hospital. To all these we wish to extend thanks. The cost of this investigation was partly defrayed by an expenses grant from the Medical Research Council, which also provided one of us (C. H. S.-H.) with a grant for scientific assistance.

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The British Social Hygiene Council has arranged to hold summer schools in Devon and France this summer. The first will be from July 31 to August 14 at the Seale-Hayne Agricultural College, Newton Abbot, Devon, where a course will be given on "Biology and Rural Life." It is intended for teachers of biology, agricultural students, social workers, and all who are interested in the social and economic conditions of the English countryside. The fee is 16 guineas. The second course will be held on August 16–30 in Paris and have as its theme "The Welfare of the Family." It is intended particularly for children's officers, probation officers, nurses, health visitors, almoners, teachers, and all who are concerned with the educational, communal, and moral aspects of family life. The family welfare services in France will also be studied. Particulars may be obtained from the council at Tavistock House North, Tavistock Square, London, W.C.1.

RECENT CHANGES IN THE DEATH RATE FROM INFLUENZA

BY

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The death rate from influenza in England and Wales has been at a relatively low level during the past decade; indeed, for rates lower than those recorded in the years 1938, 1942, 1944, 1945, 1947, and 1948 it is necessary to go as far back as the period before the epidemic of 1890–1. The explanation that immediately suggests itself for this decrease in mortality is the discovery and general use of antibiotics, which have reduced the risk of fatal respiratory complications. While such advances in treatment may well have been important, a survey of our past experience of influenza would clearly be of interest.

Mortality, 1837 to 1948

The recorded mortality of influenza, like that of other causes of death, has been affected by changes in the fashion of certifying deaths, by increasing knowledge, and also by changes in tabulation. The broad trend of the death rates, however, can be accepted for comparative purposes, attention being confined to relative deviations rather than to absolute levels. With this proviso in mind the annual death rate per 1,000,000 living since registration began in 1837 is shown in Table I. Three large outbreaks, it will be seen, divide these rates into distinct parts with differing trends.

The first large outbreak of influenza after the introduction of registration occurred in 1847–8, with a death rate of 459 per million in the latter year. The death rate remained relatively high during the following decade, and there were small peaks in 1851 and 1855, when the rates were 122 and 193 per million respectively Mortality then declined fairly steadily during the next thirty years until influenza as a recorded cause of death almost disappeared. In the nine years 1881–9 only 821 deaths were attributed to it. This position was abruptly upset by the epidemic of 1890–1. The death rate remained very high in 1892, and this outbreak clearly marks a distinct change in the trend of mortality. During the ensuing twenty-five years influenza maintained itself as an important cause of death, producing an annual mortality rate varying from 504 per million in 1900 to 120 in 1911.

In this setting the pandemic of 1918–19 appeared and produced crude death rates of 3,129 and 1,217 per million in these two years. Subsequently, influenza epidemics seemed to follow a two- to four-year cycle. Thus there were outbreaks with a death rate exceeding 400 per million in 1922, 1924, 1927, 1929, 1933, and 1937, and the actual number of deaths in these years varied from 18,635 in 1937 to 29,084 in 1929.

During 1920–30 the annual death rates oscillated considerably, but in the inter-epidemic years the rate was falling almost continuously to a lower level, although the epidemic levels showed no such falling off. From 1930 onwards, however, there has been a distinct damping down of the oscillations, while the fall in the inter-epidemic death rate has also continued. Thus the four lowest rates in the years 1920–9 lay between 196 and 237 per million, while in 1930–9 they ranged from 108 to 141.

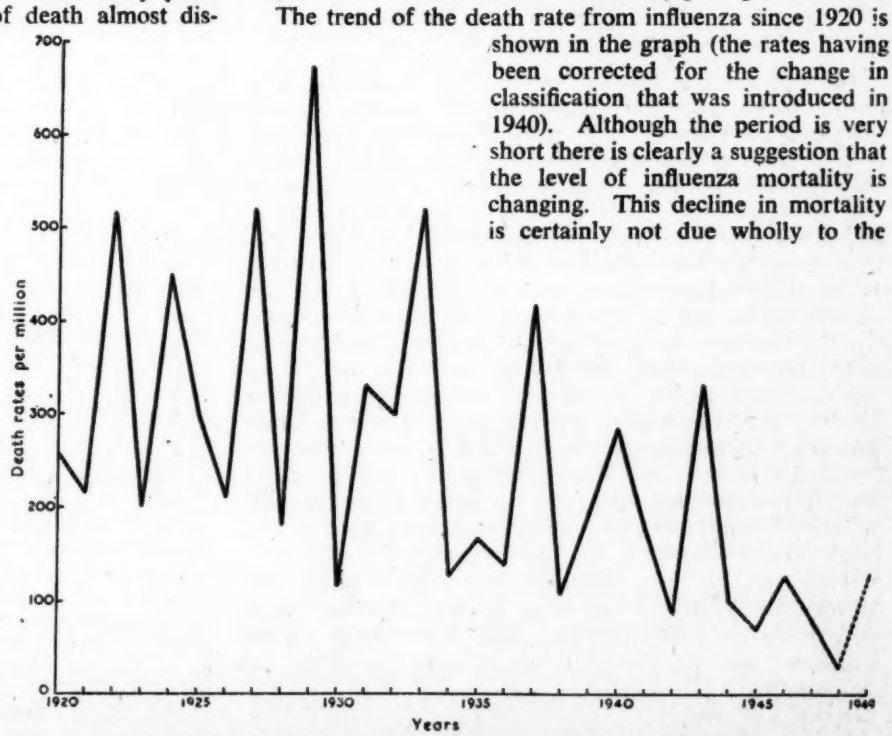
In the war years there were two peaks in mortality, in 1940 and 1943. Nevertheless, in both these years the epidemic level was substantially lower than it was in the inter-war years, in spite of the environmental factors of the time, which might well, it was feared, lead to a serious epidemic if not to a repetition of 1918–19. In the next five years, 1944–8, mortality was at a still lower level, and though some rise in the death rate will certainly be shown in 1949 it can be estimated from the experience of the first quarter that a rate of only about 135 per million is to be expected. This will be lower than any peak prior to 1944.

The trend of the death rate from influenza since 1920 is shown in the graph (the rates having been corrected for the change in classification that was introduced in 1940). Although the period is very short there is clearly a suggestion that the level of influenza mortality is changing. This decline in mortality is certainly not due wholly to the

TABLE I.—*Influenza in England and Wales. Death Rates per 1,000,000 Living*

Year	Rate	Year	Rate	Year	Rate	Year	Rate
1838	53	1868	14	1895	422	1922	563
1839	57	1869	32	1896	121	1923	220
1840	66	1870	27	1897	195	1924	489
1841	104	1871	15	1898	330	1925	327
1842	55	1872	12	1899	389	1926	229
		1873	12	1900	504	1927	567
1847	285	1874	10	1901	174	1928	196
1848	459	1875	19	1902	224	1929	734
1849	92	1876	8	1903	190	1930	126
1850	78	1877	8	1904	169	1931	330
1851	122	1878	8	1905	205	1932	300
1852	76	1879	10	1906	184	1933	520
1853	99	1880	7	1907	267	1934	127
1854	58	1881	4	1908	288	1935	167
1855	193	1882	3	1909	254	1936	141
1856	55	1883	4	1910	182	1937	418
1857	73	1884	3	1911	120	1938	108
1858	93	1885	5	1912	147	1939	194
1859	57	1886	3	1913	175	1940	286
1860	58	1887	3	1914	161	1941	177
1861	38	1888	3	1915	293	1942	88
1862	45	1889	2	1916	252	1943	333
1863	45	1890	157	1917	213	1944	103
1864	39	1891	574	1918	3,129	1945	70
1865	29	1892	534	1919	1,217	1946	130
1866	31	1893	325	1920	282	1947	79
1867	29	1894	220	1921	237	1948	29

NOTE.—Deaths were not published by causes for the four years 1843–6.



Graph showing death rates from influenza in England and Wales.

use of antibiotics, although it may have been accelerated by it, as it seems that the death rate has fallen since, at least, 1929. A continuation of the present trend will result in influenza again ceasing to be a major cause of death as in the years immediately preceding 1890–1. Faced with the rates of Table I, however, it would be singularly rash to prophesy, and no simple formula could have any value for prediction.

The Epidemic Curve

The weekly returns of deaths from influenza in the great towns of England and Wales are our only source of information on the shape of the epidemic curve. These show that the maximum of an outbreak, as measured by death, almost invariably falls in the first quarter of the year. Following the pandemic of 1918 the week of the maximum varied, but since 1936 it has been remarkably constant. The week of the maximum and the number of deaths registered during this week for the past thirty years are shown in Table II.

TABLE II.—*Influenza Deaths in the Great Towns*

Year	Week of Maximum	No. of Deaths in Week of Maximum
1920	12	392
1921	9	167
1922	4	1,450
1923	19	207
1924	10	730
1925	11	304
1926	15	302
1927	8	1,023
1928	12	135
1929	9	2,183
1930	9	102
1931	8	546
1932	1 and 2	412
1933	4	1,934
1934	11	115
1935	14	184
1936	8	119
1937	4	1,155
1938	2	91
1939	8	285
1940	8	629
1941	7	324
1942	4	90
1943	4	125
1944	49 of 1943	1,148
1945	5	89
1946	6	304
1947	6	211
1948	53 of 1947	35
1949	11	360

The year 1948 is included for the sake of completeness, but in fact a seasonal rise to a peak did not occur in that year, and the disease was only slightly above the endemic level during its first quarter. Table II shows that the variability of the date of the maximum decreased during the period until in 1936 to 1943 it became practically constant at between two and eight weeks. On the other hand, since 1943 the regularity of the trend of influenza seems to have been interrupted. The 1944 outbreak was exceptional in time of occurrence, with a maximum occurring in the last weeks of 1943. In the following year, 1945, the seasonal rise reverted to form, but in 1948 an outbreak with a definite peak did not occur at all, and in 1949 the maximum was later than any in the immediately preceding thirteen years. In the non-epidemic years the variability in the time of the maximum has been larger than in the epidemic years, and in the non-epidemic years of 1920–35 mortality seems to have taken a longer time to come to its peak than in the years after 1935.

The evidence for a change in seasonal trend is very slender, but, since three of the six years 1944–9 show more departure from the previous trend, there is at least a suggestion that the periodicity of influenza mortality may be changing. We are, as already pointed out, limited to the study of mortality. It may be that a varying fatality rate accompanies epidemics, which would explain some of the irregularities that occur both in the annual rates and in the seasonal changes.

The Age Distribution of Mortality

As is well known, one of the most striking features of the pandemic of 1918–19 was the severity with which it fell upon young adults. This remarkable change from the normal incidence of mortality was a feature of the pandemic only, and in the following years the curve of mortality at ages immediately returned to its usual shape. The incidence of mortality by age in England and Wales since then has been one of a relatively high rate in infancy falling to a minimum at ages 10–14 and then steadily increasing throughout life. During this period the mortality from influenza has fallen by half, but the rate of decline has varied at different ages. The improvement in mortality has been less in infancy, late middle life, and old age than in childhood and early adult life. The rates are shown in Table III, together with their relative changes.

TABLE III.—*Influenza Death Rates per Million. England and Wales*

Period	Ages 0–	5–	10–	15–	25–	35–	45–	55–	65–	75+
1920–4	418·3	71·2	52·8	120·6	206·4	264·5	375·1	715·9	1,537·3	3,094·8
1925–9	369·4	62·4	46·1	96·7	141·2	271·6	413·4	764·7	1,896·9	4,642·8
1930–4	240·3	42·0	33·0	70·8	102·3	199·7	329·3	534·2	1,123·1	3,349·4
1935–9	152·7	24·3	20·9	44·3	64·6	121·6	228·7	422·4	818·9	2,240·0
1940–4	150·2	16·5	13·3	32·8	42·3	75·7	156·4	320·7	657·4	1,895·4
The death rate in each age group expressed as a percentage of the death rate in 1920–4:										
1925–9	88·3	87·6	87·3	80·2	68·4	102·7	110·2	106·8	123·4	150·0
1930–4	57·4	59·0	62·5	58·7	49·6	75·5	87·8	74·6	73·1	108·2
1935–9	36·5	34·1	39·6	36·7	31·3	46·0	61·0	59·0	53·3	72·4
1940–4	35·9	23·2	25·2	27·2	20·5	28·6	41·7	44·8	42·8	61·2

Mortality at all ages in the second quinquennium, 1925–9, was higher than it was in the first, 1920–4, the crude rates being 411 and 358 per million respectively, the former mainly due to the large epidemics in 1927 and 1929. The increase in mortality in 1925–9 fell solely upon older persons, and the death rates in each age group under 35 were, in fact, lower in 1925–9 than they were in 1920–4. It is at each age over 35 that the 1925–9 rates are higher. The rates for 1940–4 are not strictly comparable with those of preceding years, since the method of classification and tabulation of joint causes of death was changed in 1940, with the result that fewer deaths would be assigned to influenza than formerly. The factor for correcting the old classification is 0.917 for all ages, but this cannot be justifiably applied to individual ages.

Summary

An examination of the English death rates from influenza since registration of death was introduced in 1837 shows that the mortality curve over the last 112 years may be divided into three broad periods each of which begins with a severe epidemic. In the first period, which followed the epidemic of 1847–8, influenza (after a slight recrudescence in 1855) almost disappeared as a certifie cause of death. The 1890–1 epidemic abruptly restored it to importance, and in the second period, which then ensued, influenza remained, after some epidemic fluctuations, at a high endemic level, with a death rate in 1901–17 varying between 120 and 293 per million. The 1918–19 pandemic ushered in the third period. The early years of this period include epidemics more severe than any that preceded 1918—for example in 1927 and 1929—but since 1929 the mortality from influenza has declined until at present it is at a distinctly low level. In five recent years, 1942, 1944, 1945, 1947, and 1948 the death rate has been at a lower level than any annual rate recorded since 1890. There is a very slight suggestion, from the returns of the deaths in the large towns, that this notable decrease in mortality has been accompanied by changes in the seasonal curve of the deaths.

INFLUENZA

A STUDY OF TWO OUTBREAKS

BY

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Between January 15 and February 22, 1949, outbreaks of Virus A influenza occurred at two military training centres in the Highland district of Scotland. These centres ("A" and "B") each had an approximate strength of 1,000 men and both received intakes of 80 to 100 recruits fortnightly. In Unit A 61 cases (6%) of influenza occurred, and in Unit B 141 cases (14%) (see Table). The nine smaller units in this district, each comprising a fairly static population of trained soldiers, reported only a few sporadic cases. We were able to observe all the cases in these two outbreaks.

Details of the Outbreak

	Duties	Time at Unit	Quarters	No. at Risk	No. of Cases	% Affected
UNIT A						
No. 1 Coy.	Recruits under training	Less than 10 weeks	Wooden huts; 1 window per 2 men; stove heating	140	20	14·3
No. 2 Coy.	" "	"	" "	160	21	13
No. 3 Coy.	" "	"	Stone buildings; 1 window per 7 men; central heating	150	3	2
No. 4 Coy.	Clerical and administrative	4 months to 2 years	" "	140	2	Less than 2
No. 5 Coy.	" "	"	" "	360	15	4
UNIT B						
"A" Coy.	Recruits under training	Less than 10 weeks	Wooden huts; 1 window per 2 men; stove heating	250	35	14
"B" Coy.	" "	"	" "	250	40	16
"C" Coy.	" "	"	" "	250	29	11·6
"D" Coy.	Clerical and administrative	4 months to 2 years	" "	250	37	14·8

All cases of influenza were admitted to a military hospital (Unit A) or reception station (Unit B) within the camp. Daily clinical notes were made on all patients in Unit A from the onset of the epidemic; these will therefore be presented in greater detail.

Unit A

Symptoms.—The onset of the illness was usually rapid but not dramatic, and 18 hours was the average period elapsing between the onset and the reporting of symptoms. During the acute phase of the illness the following symptoms were experienced: fever, 49 patients; headache, 49; pains in the back, trunk, or limbs, 35; cough, 31; sore throat, 27; shivering, 25; sore eyes, 13; nausea or vomiting, 6; epistaxis, 3; diarrhoea, 2. In many cases the complaint of cough was made only in reference to the headache and chest or abdominal pains, which it aggravated; in only two patients was the cough productive. Hoarseness or nasal catarrh developed after a few days in about a quarter of the cases. Distressing symptoms persisted for an average of five days, and on discharge from hospital 38 men had minor residual symptoms—dry cough, nasal catarrh, weakness, dizziness, hoarseness, or aching pains.

Signs.—None of the patients was seriously ill and no grave complications ensued. A blotchy flushing of the face with glistening eyes was the most constant feature; this flush was of a distinctly cyanotic hue in six cases. A slight injection of pharynx and fauces was noted in half the patients, but definite enlargement or infection of tonsils was present in only five. Two patients developed a catarrhal otitis media while in hospital, but this resolved without specific treatment. In six cases rales were present at one or both lung bases for over a week; these consisted of coarse-to-medium crepitations heard in both phases of respiration, uninfluenced by coughing and associated with local impairment of air entry. A chest radiograph in each of these cases revealed no focal changes and the white cell counts were within normal limits. Perhaps the most striking negative feature in this series was the relative freedom from gastro-intestinal disturbances: most of the tongues were remarkably clean, and many patients were able to take food even at the height of fever. Anorexia or vomiting did not persist beyond the first day.

Twelve patients were afebrile while in hospital. Of the remainder, the average duration of fever was 24 to 48 hours (over five days in only two cases). The average maximum temperature for the series was 101° F. (38.3° C.) (over 104° F. (40° C.) in three cases), and the fever reached its height more often in the morning or early afternoon than in the evening. Many patients showed a further spike of fever on the second day in hospital (usually the third day of the illness) after a fall of temperature on the previous evening. A lowered pulse/temperature ratio was a constant feature during the febrile stage; in the first few days of convalescence the pulse rate rarely exceeded 80 a minute, and in one-third of the patients readings of less than 60 a minute were recorded.

Convalescence.—Two patients were admitted with a recurrence of their original symptoms a few days after leaving hospital. The remainder were all seen one week after discharge from hospital; a few still had a mild upper respiratory catarrh, but all were fit and keen to return to duty. Mental depression and symptoms perpetuated by psychogenic factors did not occur in this outbreak.

Unit B

Clinical Aspects.—Patients from this unit reported sick more quickly, often within a few hours of the first symptoms. This was due in part to dizziness and faintness, which brought many straight from the parade ground. Apart from this common early symptom, the cases during the first half of the epidemic presented a clinical picture similar to those described above. Towards the latter part of the outbreak, however, the character of the illness changed and patients presented with nausea and vomiting associated with little or no fever and few respiratory symptoms. Ten men developed an illness of this type more than two weeks after recovering from an attack of the earlier variety: a different strain of virus may have been responsible for these second attacks, but Hirst tests for antibody titres were unfortunately not carried out on these men. Apart from one case of bronchopneumonia (this developed in the first week of the epidemic and responded well to penicillin), there were no serious or complicated cases in this outbreak. The average duration of illness was six days, and there were no problems in convalescence.

Laboratory Investigations

White cell counts were carried out during the febrile stage in 10 cases. All were within normal limits (4,000 to

10,000 per c.mm.), and the average of these counts was 6,300.

The Hirst test was performed in six unselected cases. Two specimens of serum were collected from each : the first was taken during the acute illness and the second 10 days later. The sera were examined at the National Institute for Medical Research, Hampstead, and at the Royal Army Medical College, Millbank. There was definite evidence of a virus A infection in all six cases ; five of them showed an antibody rise against the classical PR8 strain of A, the sixth only against a new strain from the current Continental epidemic (A/Paris PL1/49). Antibody rises in human sera are of varying specificity as against different A strains, and one cannot be certain from such a result about which particular strain was responsible for this epidemic. It should be noted, however, that the " 1949 A-prime " virus caused almost all the influenza in Western Europe last year, from Italy to Iceland.

Treatment

All patients were detained in hospital or reception station beds until at least 24 hours after fever and distressing symptoms had subsided ; they returned to full duty within a week of discharge from hospital. Tab. codeine co., tab. acid. acetylsalicyl. et phenacet., or a codeine linctus when cough disturbed sleep provided a satisfactory relief of symptoms, and chemotherapy (penicillin or sulphadiazine) was given to those patients with signs of bronchitis.

The following prophylactic measures were adopted: immediate isolation of cases, opening of barrack-room windows, spacing of beds, and sprinkling of floors before sweeping. The training programme was not modified, and the movement of troops to, from, and within the camps was not restricted.

Epidemiological Features

The epidemiology of Virus A influenza in military units has been studied by Stuart-Harris (1945) in England and by the Commission on Acute Respiratory Diseases (1948) in America. The variability of outbreaks is emphasized in both these reports. This may be due to differences in the host, the infective agent, or environmental conditions. Stuart-Harris notes the potent effect of a frequent change of population in prolonging an epidemic, and records a higher incidence of influenza among recruits with the shortest residence in the community. The American workers found that the incidence among recruits and seasoned men was the same under comparable living conditions, and considered that environmental factors were mainly responsible for differences in the outbreaks which they studied.

We shall consider the incidence of cases in our series in the light of these observations.

Influence of Recruits

The Chart shows that, although the average daily incidence of cases was approximately the same in both units, the outbreak was confined to 13 days in Unit A but persisted for over 30 days in Unit B. The first two intakes of recruits to Unit B may have played some part in prolonging that epidemic, but these recruits did not experience a higher incidence of cases than the other men, and the third intake on February 17 escaped completely. Recruits arriving at the peak of the outbreak in Unit A did not affect the course of that epidemic, and none contracted influenza. The American workers also record the escape of an intake of

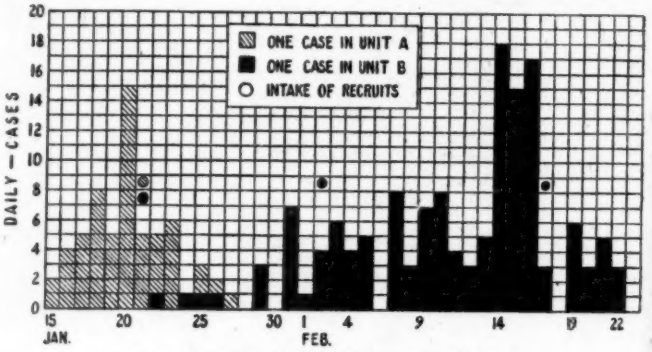

Chart showing daily incidence of influenza.

recruits at the height of an epidemic, and attribute this to a previous exposure to infection ; antibody studies indicated that these men were largely immune.

Although Unit B contained a larger proportion (75%) of recruits than Unit A (45%), this was not directly responsible for the greater extent of the outbreak in Unit B, where the incidence among recruits and seasoned troops was the same. In Unit A there was a higher rate of infection among recruits than among seasoned troops, but the living conditions of the two groups were not comparable (see below).

The Infective Agent

An increase of upper respiratory infections (common cold, tonsillitis, pharyngitis, etc.) was noted during the fortnight preceding the influenza epidemic in Unit B (57 cases), but not in Unit A (17 cases) It is possible that infections of similar aetiology were diagnosed as influenza during the succeeding epidemic, and this may have contributed to the greater extent of the outbreak reported in Unit B. The occurrence of two clinical types in Unit B also suggests that more than one infective agent was active in this epidemic—either a non-influenzal organism or a variant of the predominant influenzal strain. This agent may have been introduced from the local town, where influenza was epidemic during the same period. Unit A was stationed 13 miles from the nearest town, and influenza was not epidemic in the surrounding villages.

Environmental Conditions

The table shows that the incidence of infection was 11.6–16% in six of the companies and 4% or less in the three other companies. These three companies (all in Unit A) were quartered in central-heated stone buildings, whereas the remainder occupied better ventilated but colder stove-heated huts. Although the total incidence of influenza in Unit A was higher among the recruits than among seasoned troops, this difference was not found where the living conditions of the two groups were comparable : No. 3 company of recruits, housed in the stone buildings, escaped with only three cases of influenza.

Living conditions thus appeared to influence the incidence of influenza, but cross-infection in " high-incidence " quarters was not a marked feature of this epidemic. In the outbreak reported by Milne and Cruickshank (1949), only one patient stayed in his quarters for over 24 hours, and 18 of his 20 comrades in the same hut developed influenza. In this epidemic fewer than five other cases developed in each of the 11 huts (20 men per hut), where men with influenza remained overnight and charts of bed positions revealed no significant evidence of bed-to-bed infection. Where a number of cases developed simultaneously it was usually found that they had all been

exposed to the same adverse conditions : nine soldiers developed symptoms within a few hours of a five-mile march in heavy rain, and other groups attributed their illness to a chilling consequent upon the over-zealous opening of windows in the sleeping quarters.

Stuart-Harris suggested that meteorological factors might determine the onset of an influenzal outbreak. We therefore obtained details from local Air Force stations of the conditions prevailing during January and February, 1949. No dramatic changes of temperature were associated with the onset or the peak of either epidemic, but rain fell on each day of the week preceding the peaks of both epidemics.

Discussion

These two outbreaks differ from those commonly reported in this country (Stuart-Harris, 1945) in that recruits and seasoned men were equally affected when living under comparable conditions. This finding suggests that the community had no recent experience of the infective agent. The new antigenic strain of virus which we reported had rarely been experienced in this country and would have been expected to provoke an equal incidence among recruits and trained men. We did not prove, however, that this strain was responsible for the epidemic as a whole. Furthermore, the American workers claim that the incidence of Virus A influenza of the usual antigenic types is not determined by the duration of residence in the community. This implies that Virus A influenza may not be an endemic disease. The behaviour of future epidemics in this country may be of interest in this connexion, but no definite conclusions can be drawn from the limited evidence which we have presented.

Differences of environment rather than of host susceptibility determined the variability of the American outbreaks, and overcrowding was responsible for the higher infection rate in certain groups. Our experience is similar, but exposure to cold seemed to play a greater part than cross-infection.

Summary

The incidence of influenza (Virus A) among troops in the Highland District of Scotland during January and February, 1949, is reported.

Epidemics were confined to two training centres. The form of these two outbreaks and the factors affecting the incidence and spread of infection are discussed.

Clinical features, laboratory investigations, and treatment are also described.

We wish to thank the Director-General of Army Medical Services for permission to publish this paper, and Dr. W. S. Sutton for his helpful criticism.

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The Ministry of Health states that gifts of blood to the National Blood Transfusion Service for hospitals in England and Wales during the quarter ending September 30, 1949, were the highest since the war. They totalled 116,021, as against 95,301 in the comparable quarter last year. New donors enrolled in the quarter numbered 37,219. Also a post-war record was the total strength of the donor panels—376,502, or 9,335 more than a year ago. For the Welsh Blood Transfusion Region alone the figures for the quarter (with those for the comparable quarter in 1948 in parentheses) were: Donations, 4,005 (3,022) ; new donors 1,617 (866) ; strength of donor panel, 12,417 (11,421).

AUREOMYCIN IN TREATMENT OF PERITONITIS

BY

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Recent observations have shown that the mortality encountered in peritonitis secondary to appendicitis, perforated peptic ulcer, and penetrating wounds of the abdomen has been reduced 60% by the post-operative use of variable combinations of sulphonamides, penicillin, and streptomycin (Altemeier, 1949 ; Pulaski, Voorhees, and Seeley, 1949). In spite of the better prognosis thus afforded, the case fatality is still between 5 and 10%. Consequently the search for more effective antibiotics to add to the surgeon's armamentarium continues. The new antibiotics chloramphenicol (" chloromycetin ") and " aureomycin " have been used successfully in the treatment of generalized peritonitis incident to intestinal perforation complicating typhoid fever (Woodward, Smadel, and Ley, 1949), and in appendicitis and in carcinoma of the urinary bladder (Yeager, Ingram, and Holbrook, 1949).

During the course of recent investigations by the United States Army Medical Research Unit in Malaya several cases of generalized peritonitis were treated with the two new drugs. Those which received chloramphenicol are discussed in another article (Smadel, Bailey, and Lewthwaite, to be published). The present report summarizes the observations made on five patients treated with aureomycin who were suffering from peritonitis secondary to perforating lesions of the gastro-intestinal tract.

Clinical Observations

Three cases in the present group had acute appendicitis which resulted in rupture and peritonitis. Two of these three had generalized abdominal disease when in hospital. The third case was observed throughout the course of the illness but refused to grant permission for operation until after rupture had occurred ; the fourth case developed peritonitis following perforation of a peptic ulcer ; while the last of the group suffered perforation of the intestine late in the course of typhoid fever. Exploratory laparotomy and appropriate surgical procedures were done as soon as possible in the first four cases. The individual with the perforated typhoidal ulcer was treated with aureomycin alone without benefit of surgery.

Aureomycin (" duomycin ")* was administered in the form of gelatin-coated capsules. Treatment was started one to three days after signs of peritonitis had appeared—that is, one to twenty-four hours after surgery was performed in those cases operated on. In general, an initial oral dose of 3 g. of aureomycin was given, followed by 0.25 g. every two hours for two days and then by 0.25 g. every four hours for the succeeding three to five days. Water in small amounts was administered along with the capsules during the acute phase of the disease.

Routine clinical and laboratory observations were made on the patients. Bacteriological studies were limited and no attempt was made to identify the bacterial flora of

*Aureomycin (duomycin) was supplied by Lederle Laboratories Division, American Cyanamid Company.

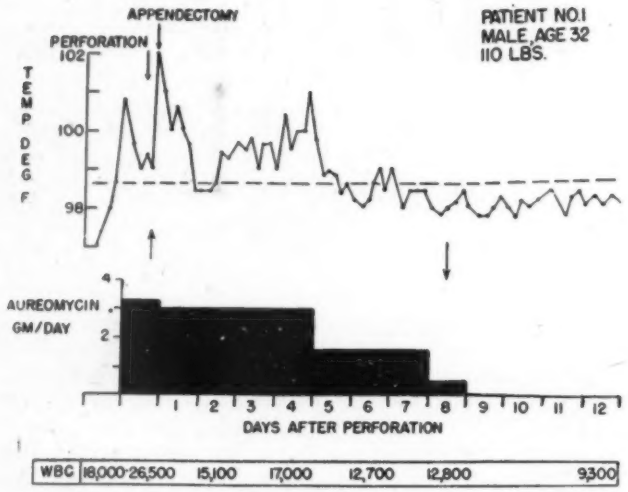

FIG. 1.—Clinical response of patient with peritonitis secondary to ruptured appendix (Case 1). Aureomycin therapy was instituted following appendicectomy.

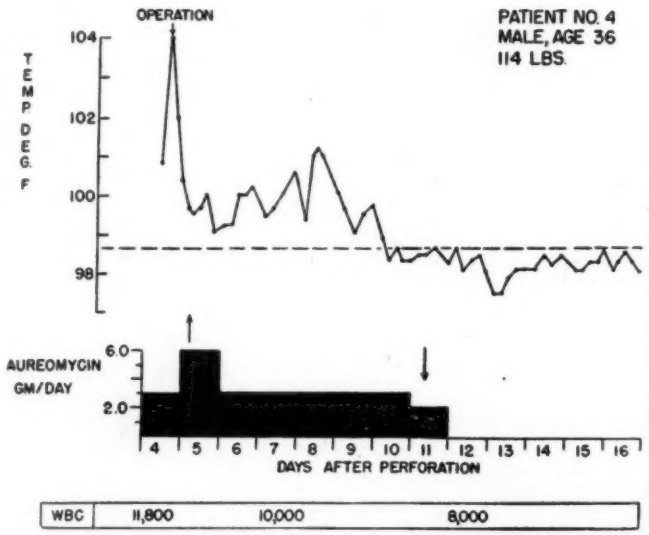

FIG. 2.—Clinical response of patient with generalized peritonitis secondary to perforated pyloric ulcer (Case 4). Aureomycin therapy was begun promptly after closure of the perforation.

peritoneal exudate obtained at the time of operation. The diagnosis of typhoid fever for Case 5 was established by the cultivation of *Salmonella typhosa* from the faeces after he had recovered from peritonitis.

At the time of operation each of the three cases of appendicitis had a perforated gangrenous appendix with faecal contamination of the peritoneum. Recovery was rapid in these three following appendicectomy and the institution of aureomycin therapy. The toxic signs and symptoms began to subside within one day and the patients were afebrile within four to five days. Convalescence was uneventful in Case 2. Cases 1 and 3 suffered recurrent infection. Case 1, whose record is summarized graphically in Fig. 1, developed an infected haematoma in the abdominal incision, which responded promptly when superficial drainage was effected on the 14th day. Case 3 developed a tender mass in the right iliac fossa 13 days after antibiotic therapy was discontinued. A second laparotomy revealed a localized abscess, and at this time abdominal drainage was carried out. Aureomycin was not given after the second operation, and it is worthy of note that the febrile period in this instance was two days longer than after the first surgical intervention.

Case 4 had an antecedent history suggestive of peptic ulcer. Perforation of the ulcer, as evidenced by sudden onset of abdominal pain with subsequent distension and frank signs of peritonitis, undoubtedly occurred three days before entry into the hospital. Laparotomy performed shortly after admission revealed a perforating lesion in the anterior pyloric region with a considerable amount of purulent exudate in the peritoneal cavity. The perforation was closed by suture. Aureomycin therapy was begun about six hours post-operatively. Gastric drainage was maintained by a Ryle's tube, which was left in place. Following aspiration of the contents of the stomach, aureomycin, which had been removed from the capsules and suspended in a small amount of water, was administered by means of the tube. The record of Case 4 is summarized graphically in Fig. 2. Twenty-four hours after operation the abdomen was no longer rigid, and by the sixth day the temperature had returned to normal. Convalescence was uneventful, and the patient was discharged on the 16th day.

Case 5 was admitted to hospital *in extremis* on the 21st day of an illness diagnosed clinically as typhoid fever. Signs of intestinal perforation and generalized peritonitis of three days' duration were present. Laboratory confirmation of the diagnosis of typhoid infection was established late in the disease. Surgical intervention was considered to be inadvisable, as the patient's condition was so poor that it was thought he would not survive an operation. Aureomycin therapy, administered by a gastric tube, was begun three hours after admission. Supportive treatment was given in the form of parenteral fluids and intubation of the stomach and rectum. There was daily improvement in the patient's condition until by the sixth day of hospital treatment abdominal distension had disappeared and bowel movements occurred with normal frequency. Throughout this period and for an additional two weeks the temperature ranged between 99 and 102° F. (37.2 and 38.9° C.). However, after the first week in hospital, the patient was free of signs or symptoms suggesting peritonitis. Repeated cultures of blood, urine, and faeces were negative until the sixth week of observation, at which time two samples of faeces yielded *Salm. typhosa*. Aureomycin therapy had a profound effect on the peritonitis present at the time of admission, but the typhoid infection, which was the basic disease, was apparently unaffected. Aureomycin is known to have little, if any, effect on typhoid fever (Bryer, Schoenbach, Chandler, Bliss, and Long, 1948; Knight, McDermott, and Ruiz-Sanchez, 1949; Woodward, Smadel, and Ley, 1949).

Data on the five cases are presented in the accompanying Table.

Details of Cases

Case No.	Cause of Peritonitis	Duration of Peritonitis before Antibiotic Therapy (days)	Aureomycin Therapy: Total Drug (g.)	Aureomycin Therapy: Duration (days)	Duration of Fever After Antibiotic Started (days)	Result	Days in Hospital
1	Perforated gangrenous appendix	1	20·5	7·5	6	Recovery	38
2	"	2	19·2	7·5	5	"	26
3	"	1	19·5	5·0	4	" (abscess RLQ)	34
4	Perforated pyloric ulcer	3	25·5	6·5	5	Recovery	16
5	Perforated typhoid ulcer (not operated)	3	30·5	7·0	21	"	56*

* See text.

Summary

Five cases of generalized peritonitis secondary to perforating lesions of the gastro-intestinal tract were benefited by treatment with aureomycin. Four of these received the drug post-operatively; the fifth recovered without surgical intervention.

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EPITHELIOMA AND PAPILLOMA ARISING ON RECENTLY IRRADIATED SKIN

REPORT OF THREE CASES

BY

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[WITH PHOTOGRAVURE PLATE]

Hyperkeratosis and epitheliomatous degeneration are well recognized as late complications of chronic radiodermatitis following treatment. Typically they develop on a basis of obvious skin damage such as atrophy, telangiectasia, epidermal thickening, etc., though they may at times be caused by repeated irradiation over several years without obvious skin reaction. The latent interval is usually several or many years; MacKee and Cipollaro (1937) state that *x*-ray epithelioma has been seen as early as two years after excessive irradiation. The same authors (1946) refer to epithelioma shown to occur within a year after the healing of a third-degree reaction—that is, an "acute necrosis" involving the true skin (dermis).

The following cases, occurring a very few months after *x*-ray reactions of only moderate severity (second degree, with shedding of epidermis only), therefore seem to be worthy of record.

Case 1

Mr. A., aged 65, had carcinoma of the larynx involving the left cord and anterior commissure. Biopsy from the cord had shown a Grade 3 squamous epithelioma (Plate, Fig. 1). No secondary nodes were felt.

Treatment was given by *x* rays at 200 kV, H.V.L.=1.5 mm. Cu, filter of 1 mm. Cu and 1 mm. Al, 40 cm. F.S.D.; output (for 8 by 6 cm. field, including backscatter) 60 r per minute. Two principal parallel fields were used, with the aid of a wax mould which served the double purpose of acting as a "beam director" and filling in the air gaps. From December 28, 1946, to January 21, 1947, these two fields were treated daily to a total of 3,450 r incident dose on each (initial dose of 300 r, then 9×350 r)—24 days overall; treatment was continued from January 23 to 28 by an 8 by 6 cm. field from the back, to 1,200 r incident (3×400 r). Total treatment time was therefore 31 days, the estimated tumour dose was 4,600 r, and the skin dose at the sides of the neck approximately the same. The skin reaction proceeded to a deep erythema with dry desquamation and a few small moist patches. Healing was rapid and uneventful.

Seven weeks after the end of treatment there was no trace of the primary lesion, the site of which was marked by a pale scar; the case notes record "little skin change" in the neck. In June, 19 weeks after treatment, "a little atrophy and pigmentation in the treated region" was noted; in the middle of the field on the right side was a skin nodule 7 mm. across, which according to the patient (an intelligent observer) had been present five weeks. A month later it had grown to 9 mm.; the accompanying photograph (Fig. A) shows its appearance at that time. It was therefore excised and sectioned; the histological report stated: "The section shows the structure of a simple squamous papilloma, which has been completely removed" (Fig. 2). The patient has remained well to date, after 26 months.

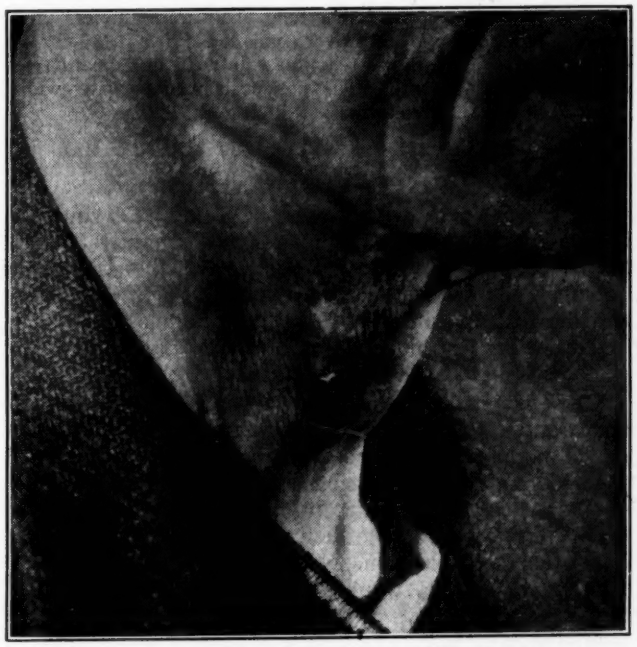

FIG. A.—Case 1. External lesion in July, 1947: simple squamous papilloma.

Case 2

Mr. B., aged 72; carcinoma of hypopharynx (right arytenoid region), with a hard fixed secondary mass of nodes 4 by 2.5 cm. below the angle of the jaw on the right side. A "needle biopsy" (Ellis and Hermitte, 1947) from the nodes showed "several portions of a Grade 2 squamous epithelioma, in a mixture of blood and acute inflammatory exudate" (Fig. 3).

Treatment.—The same factors were employed as in Case 1. Two parallel fields were used, each 10 by 8 cm. to include primary and nodes. Between February 14 and March 19, 1947, 3,000 r was given to each field, by treatment on alternate days (12×200 r, then 2×300 r), both fields being irradiated at each session; the overall time was 33 days. The skin dose was estimated to be 3,900 r, and the dose at the primary about the same. The skin reaction was an erythema of moderate depth. Primary and nodes regressed to a considerable extent, but 11 weeks after the end of treatment a nodule 1.5 cm. across was noted within the treated field on the left side. This was excised, and the section report stated: "Grade 1 squamous epithelioma which appears to be primary skin growth. Completely removed" (Fig. 4). One year after treatment the patient died from the effects of the primary lesion.

Case 3

Mr. C., aged 76; secondary nodes in neck, primary uncertain. There was a large hard fixed mass of nodes below the angle of the jaw on the right, 6 by 3.5 cm. Needle biopsy showed "rather undifferentiated malignant cells, probably anaplastic squamous carcinoma" (Fig. 5).

Treatment, with the same general factors as above, was by the "wedge field" method described by Ellis and Miller (1944), using two fields of 8 by 6 cm. at a right-angle. Daily treatment between August 31 and September 23, 1948, gave a total of 3,500 r incident on each field (17 × 200 r, 1 × 100 r); the depth dose was about 3,500 r and the skin dose approximately the same; the overall time was 23 days. A moderate erythema developed, and the mass decreased in size to 3 cm.

Seven weeks after the end of treatment a nodule 2 cm. across was noted on the lower part of the right cheek within the treated skin area, which showed no gross changes; the patient thought it had been present for two weeks. A biopsy was taken, which showed "a portion of a cornifying Grade 1 squamous epithelioma" (Fig. 6). It was decided to treat by r rays, at 100 kV, H.V.L.=2 mm. Al; filter of 1 mm. Al. F.S.D.=15 cm., with a circular field of 3 cm. diameter. 500 r was delivered twice weekly to a total of 3,500 r in 23 days in seven fractions. A moist reaction followed, and healing was complete after a month. The patient is well to date, with a residue of the secondary mass still present.

Discussion

All three cases show very similar features, with squamous skin lesions appearing within weeks after moderate radiation reactions. If the patients' own observations be accepted, the intervals between the end of the treatment and the first appearance of a definite nodule were 14, 11, and 5 weeks respectively. Various possible explanations of these lesions have to be considered.

(*a*) *They May be Skin Secondaries.*—The clinical appearances were typical of primary skin tumours and unlike nodules of secondary growth, which are usually subepidermal or subcutaneous. In Case 1 the histological grade was lower than that of the primary lesion, and in Cases 2 and 3 it was lower than that of the secondary nodes. It is often said that a metastasis is invariably of the same grade as the primary, or a higher grade; if so, this is a strong argument against the possibility of the lesions being skin secondaries in these cases (though I have observed one case in which a Grade 2 epithelioma of the tongue gave rise to a secondary node in the submaxillary region which was of a highly cornifying Grade 1 character). But the most convincing argument against this possibility is the actual microscopical appearance in each case, which is perfectly typical of a primary skin tumour and quite unlike that of a skin secondary (see Figs. 2, 4, 6).

(*b*) *They May be Coincidental.*—If an early microscopic skin tumour was present before the start of radiotherapy the dosage given to the skin in each case would be expected either to be curative of such tumour or at least to delay its appearance very considerably. If, on the other hand, the tumours originated after the radiotherapy had been completed, then the latent interval before their clinical appearance would be extremely short, especially in the third case, in which the interval was seven weeks at most, more probably five. In pitch or tar workers the shortest latent period in the series of Henry (1947) was eight months for a papilloma and ten months for an epithelioma. Once initiated, however, epitheliomas can grow very rapidly; Winternitz (1947) mentions a squamous carcinoma in a pitch worker that had apparently grown from microscopic size to 0.7 cm. in diameter in a fortnight at most. A carcinogenic "stimulus" which would take many months or years to produce an epithelioma on "normal" skin might perhaps produce the same effect in a few weeks in the case of skin that had undergone the abnormal changes of acute radio-dermatitis. If this were so, cases similar to ours should not be extremely rare, yet they do not appear to have been recorded.

(*c*) *They May be "Late" Radiation Effects.*—Late radiation effects typically follow definite overdosage, leading to gross skin changes, both naked-eye and microscopical. Histologically there is dense fibrosis of the corium, with thickening and obliteration of blood vessels. In none of these respects do the present cases correspond.

(*d*) *They May be "Early" Radiation Effects.*—(i) A possible explanation might be based on the action of *x* rays upon chromosomes. It is well recognized that mutations can be produced experimentally by radiations, and such a mutation in one or more cells due to the radiation treatment might theoretically be the starting-point of a new growth. The whole question of somatic mutations as possible factors in carcinogenesis is still speculative: but if this explanation were correct then radiation-induced epitheliomas would not be excessively rare after the scores of thousands of skin fields treated by *x* rays. Much more convincing evidence would be required before such an explanation could be entertained. (ii) The radiation itself may be responsible for the tumours—that is, act as an "acute" carcinogen in the same way as other carcinogenic agents. The latent periods of 7, 11, and 19 weeks are surprisingly short for human carcinogenesis, but exceptionally early cancers have been known to occur—for example, the case recorded by Bang (1923) in which a carcinoma appeared on a workman's nose 16 days after a splash of hot tar. This explanation also faces the same difficulty as the last—that is, the extreme rarity of the sequence. (iii) One may also consider the possibility of an associated carcinogenic irritant such as a local application to the skin. Attention has been drawn to the possible carcinogenic effect in humans of prolonged application of liquor picis carbonis (Berenblum, 1948); the combination of two irritants might have a more rapid effect than either separately. The only local application used in our cases was penicillin cream, for periods up to about two weeks.

Summary

In this paper are described two cases of squamous epithelioma and one case of papilloma, appearing on the skin at intervals of 7, 11, and 19 weeks after completion of radical *x*-ray therapy, with moderately severe skin reactions. Several possible explanations are discussed.

I am grateful to Dr. L. C. D. Hermitte, pathologist to the United Sheffield Hospitals, for the histological details; to Dr. I. Berenblum, of the National Cancer Institute, U.S.A., for helpful comment; and to Mr. L. R. Reeves, F.I.M.L.T., principal laboratory technician at the Centre, for the photomicrography.

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The Ministry of Health has sent a circular to hospital boards and committees asking them to help tuberculous persons find suitable work, whether as nurses or otherwise, in tuberculosis sanatoria. This has already been done at many tuberculosis institutions. Though there may be some administrative disadvantages in employing tuberculous nurses or other staff in sanatoria, the Minister considers that the advantages outweigh them. Patients nursed by these people find an exceptional degree of sympathy and understanding.

A CASE OF ACUTE PORPHYRIA

BY

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Three years ago a patient with severe abdominal pain and nervous lesions was admitted to hospital. Laboratory investigation established a diagnosis of acute porphyria. A sample of porphyrin was obtained from the urine, but was not subjected to detailed examination at that time.

In view of recent interest in this rare condition—e.g., Hare and Wilmore, 1948; Petrie, 1948; Davies, 1949—and particularly in view of the suggestion by Discombe (1948) that cases might be looked for in Northern Ireland, it seemed desirable to investigate this patient in more detail and record our findings.

Case Report

The patient, a girl aged 17, had had attacks of dull cramp-like para-umbilical pain for the previous four to five years. These attacks coincided with the beginning of the menstrual period and usually lasted from 12 to 24 hours. The attacks were stated to have shown a tendency to increase in severity as she got older. They were seldom accompanied by vomiting, but obstinate constipation was a constant feature. The periods were regular, occurring every 21 days and lasting for seven days. About 18 months previously there had been a mild attack of jaundice lasting for three weeks.

Two days before admission to hospital, on the fifth day of her menstrual period, the patient had a severe and protracted bout of abdominal pain and went to bed. Later that day, on getting up, she felt weak, and found that her limbs were shaking to such an extent that she could not control them. By the next day the tremor had passed off, but she still felt ill and the severe abdominal cramps recurred frequently. The spasms lasted for some minutes and recurred approximately every half-hour. The pain, dull and colicky in nature and situated in the umbilical region, left her exhausted and weak, and she vomited on several occasions. She had been constipated since the onset of pain. The pain persisted all that night and she was admitted to hospital next day (April 10, 1946) for investigation.

The patient was a well-nourished girl of 17 years, distressed and restless but alert and co-operative. Her temperature was 98.4° F. (36.9° C.), pulse 100, and respirations 20. Pallor was pronounced; the tongue was moist and there was no evidence of dehydration. The abdominal wall was held tightly, but moved with respiration, and no rigidity or tenderness could be detected; there was no visible peristalsis. Rectal examination was negative. The cardiovascular system was normal; the blood pressure was 130/60. The lungs were clear and the central nervous system was normal. Radiographs of the abdomen showed no abnormality. Examination of the blood revealed a moderately severe microcytic anaemia. There was no leucocytosis. A fractional test meal was normal and a glucose-tolerance test showed a normal resting blood sugar and curve. No sugar was present in the urine.

The first specimen of the urine was found to be dark red in colour, with a specific gravity of 1022 and a trace of albumin. Initially it was thought that the colour was due to an admixture of blood, as the patient was still menstruating, but a subsequent catheter specimen was also dark red, gave negative tests for blood, and showed no red cells in the spun deposit. Further specimens of urine were then examined in the Biochemistry Department of Queen's University, Belfast, and a porphyrin was isolated; details are given below. During the rest of her stay in hospital the patient continued to pass dark-red or reddish-brown urine, or, on rare occasions, pale urine which darkened on standing.

On questioning, the patient stated that she had first noticed the passage of reddish-brown urine some 21 months before admission to hospital. The abnormal colour was not present constantly, nor was there any relation between the passage of abnormally coloured urine and the attacks of pain.

Progress

After the first 24 hours in hospital the patient's condition improved considerably; the abdominal pain subsided, and by the fifth day she felt fit, and was eating and sleeping well. She was, however, still passing dark red urine. On the eighth day she complained of some weakness in her arms. Examination revealed some slight loss of power in the muscles of her shoulder girdles and upper arms—equal on both sides; reflexes were normal.

By the next day weakness in the arms was more pronounced and she had some loss of power in her legs. Neurological examination on the tenth day showed flaccid weakness of both arms and legs, especially in the proximal portion of the limbs. The reflexes were diminished or absent and the plantar responses were flexor. All forms of sensation were normal and there were no subjective sensory complaints. The cranial nerves were normal. During the next few days the weakness in the arms and legs gradually became more severe, but complete paralysis did not occur.

By the fourteenth day there was some weakness of the abdominal muscles, and the patient was unable to raise her head from the pillow; voluntary cough was also weak. There were no bulbar symptoms, voice and swallowing being normal. Micturition was normal, and mentally she was alert and orientated. For the next three days the patient's condition remained stationary, but on the eighteenth day her parents, who were greatly concerned by her condition, insisted on taking her home. At that time it was felt that her chance of survival was remote.

Recently it has been possible to interview and examine the patient again and to obtain details of the course of her illness following her discharge from hospital. A few days after her return home the motor weakness in her legs became less severe and she was able to sit up in bed and lift her hands above her head. During the next week or so she continued to improve, but then relapsed and experienced a severe burning pain in her feet; this pain could be relieved to some extent by massage. So far as the patient was aware there was no impairment of sensation. With the onset of this pain the motor weakness returned rapidly to involve all four limbs once more. She remained in this helpless state, unable to move arms or legs, for some weeks, and her illness was further complicated at this time by an attack of jaundice of moderate severity. As the jaundice receded so her motor weakness gradually improved, and two months after leaving hospital the patient was able to sit up in bed unaided and move her arms and legs, although full power was by no means completely restored. Over the next three to four months her strength returned to normal, and by January, 1947, she was able to walk unaided out of doors. There were no further attacks of abdominal pain, and amenorrhoea persisted for seven months after the onset of the acute illness.

When examined in October, 1948, and again in May, 1949, the patient had no symptoms apart from periods of constipation which lasted from two to three days. Neurological examination was negative, and she looked and felt well. The urine was reddish orange to reddish brown in colour, and had been like that since she left hospital more than two years before. Menstruation was occurring every 21 days, but was no longer accompanied by attacks of abdominal pain. At the present time the patient remains well, though the urine is still abnormal in colour and contains uroporphyrin

Family History

In view of the hereditary nature of acute porphyria, careful inquiries were made regarding possible evidence of the disease in other members of the family.

The paternal grandparents of the patient were dead: the man had died of a stroke when 73 and the woman of heart disease when "elderly." The maternal grandparents were also dead: the man, of pneumonia, at 59, and the woman, of "old age," at 82. The patient's mother had a brother (aged 47) and a sister (49), both of whose urines were tested and found normal, as were those of a brother (46) and sister (48) of her father, whose other brother (54) and sister (*c.* 60) were in the United States and were said to be normal and healthy. The patient's father (51) and mother (52) showed no signs of porphobilinogen or porphyrin in their urine. Their only other child, a girl, had died at the age of 7 years after an attack of rheumatic carditis.

Laboratory Investigations

Methods.—Porphyrin spectra were measured with a Hartridge reversion spectroscope (Beck) calibrated against a mercury arc. Melting-point determinations were made with a microscope hot-stage and polarizing attachment, making it possible to use quantities of material of the order of a microgram. The apparatus was calibrated against a range of compounds of known melting-point as determined with a standard thermometer. All melting-points given in this paper are corrected.

Findings

During the acute attack in 1946 the freshly voided urine had a pink tinge. It exhibited the absorption bands of alkaline porphyrin on spectroscopic examination of a thick layer, and gave a strong pink fluorescence in ultra-violet light. It darkened on heating or on being allowed to stand. The Ehrlich reaction for porphobilinogen (Watson and Schwartz, 1941) was positive, the red pigment showing two absorption bands (at 561 and 500 mμ). This pigment was insoluble in chloroform. The Schlesinger test was negative. Ether extraction of the urine acidified with acetic acid gave very little coproporphyrin. A preparation of uroporphyrin made from 2 litres of urine by the barium adsorption method of Chandler, Harrison, and Rimington (1939) gave 9 mg. of crystalline uroporphyrin methyl ester melting at 263° C.

Three years after the acute attack described above the appearance and reactions of the urine remained the same, except for the absence of porphyrin absorption bands (viewed in a layer of 8 cm.) and the absence of pink fluorescence in ultra-violet light. Ether extraction of a sample (100 ml.) of urine acidified with acetic acid gave only traces of coproporphyrin as judged by the fluorescence of an HCl extract of the ether.

Uroporphyrin was isolated from the urine by the following method. 2.5 litres of fresh unheated urine were brought to *p*H 3.7 with glacial acetic acid and stirred with 50 g. of talc (B.D.H., "acid-washed"). The talc was filtered off, washed with a little dilute acetate buffer *p*H 3.7, and the porphyrin together with a considerable amount of impurity eluted with two 40-ml. portions of N/1 ammonia. The combined eluates were brought to *p*H 3.7 with concentrated HCl and allowed to stand for an hour. The precipitate was filtered off, the filtrate stirred with 5 g. of talc, and the porphyrin eluted with 25 ml. of ammonia. On bringing the eluate to *p*H 3.7 a further precipitate of porphyrin came down and was combined with the first. The combined precipitates were suspended in 5 ml. of methyl alcohol saturated with HCl gas and allowed to stand overnight. The insoluble material was centrifuged off; the supernatant was mixed with three volumes of chloroform and then with excess ice-cold water. The $CHCl_3$ layer was washed repeatedly with water, once with dilute ammonia, and finally twice with water. It was then dried over anhydrous Na_2SO_4, filtered, and evaporated to small bulk, and the porphyrin crystallized from a hot methyl-alcohol–chloroform mixture (3:1). The crystals were dissolved in a small volume of hot benzene and chromatographed on chalk. On development with benzene three porphyrin-like zones could be seen as judged by colour and by red fluorescence in ultra-violet light. The main wide band containing most of the porphyrin was separated from the rest of the column, the porphyrin eluted with $CHCl_3$ and crystallized from hot CH_3OH–$CHCl_3$ mixture. The yield was 0.63 mg. of matted hair-like crystals, m.p. 271° C. A dilute $CHCl_3$ solution showed absorption bands at 626.7, 571.8 (maximum), 536.8, and 503.0 mμ. This corresponds closely to the absorption spectrum of a uroporphyrin octamethyl ester (Grinstein, Schwartz, and Watson, 1945). This porphyrin ester was rechromatographed from a petrol-ether/benzene mixture (1:3) and developed with benzene. The main porphyrin ester from this chromatogram after recrystallization melted at 278° C. This value is close to the melting-point obtained by Grinstein *et al.* for uroporphyrin octamethyl ester Type I, isolated from natural sources.

In order to obtain definite evidence that the porphyrin was of Type I, this material was decarboxylated to the corresponding coproporphyrin by heating in a sealed tube with 1% (w/v) HCl at 185° C. The product was re-esterified, chromatographed on chalk from 1:1 petrol-ether/benzene mixture, and developed with 1:20 choloroform–benzene mixture. The main porphyrin ester from this chromatogram showed absorption bands at 622.1, 596.2, 566.9 (maximum), 533.0, 498.9 mμ, corresponding closely to coproporphyrin methyl ester (Fischer and Orth, 1937). On crystallization the porphyrin ester was obtained as needles, melting point 224–239° C., the latter temperature being the point at which double refraction was completely lost. There was not enough material for further purification. While there is some doubt about the melting-point of the methyl ester of coproporphyrin III (Jope and O'Brien, 1945), it appears to be about 150° C., and is certainly much lower than that obtained for our product, which must have been mainly coproporphyrin I ester. This, taken in conjunction with the melting-point obtained for the uroporphyrin itself, makes it clear that the main uroporphyrin in the urine was the Type I isomer.

The yield of preformed uroporphyrin (0.63 mg. from 2.5 litres of urine) obtained during this remission stage of the disease is small, though it was found that it could be increased to several times the amount if the urine were heated at *p*H 3.7 before starting the isolation.* During the acute attack the amount of uroporphyrin in the urine was much greater.

The specimens of urine from the patient's relatives were shown to be free from uroporphyrin and porphobilinogen by the following tests: negative Ehrlich test (Watson and Schwartz, 1941); failure to darken appreciably on heating or standing after acidification with acetic acid; absence of absorption bands; and absence of abnormal fluorescence in ultra-violet light.

Discussion

The clinical features of this case require little comment, for the patient presented many of the classical manifestations of acute idiopathic porphyria, including abdominal pain, constipation, vomiting, involvement of the central nervous system, and presence of uroporphyrin in the urine coupled with absence of skin symptoms and of photosensitivity. Of interest was the five-year history of recurrent abdominal colic associated with menstruation. It was felt that this pain was probably a manifestation of porphyria and not of spasmodic dysmenorrhoea, as the site and radiation were not typical of the latter condition, for in dysmenorrhoea the pain is usually felt in the lower abdomen, and radiation, when it occurs, is mainly to the sacrum and occasionally into the thighs (Holland, 1937). Moreover, the patient's pain, which occurred at the time of the menstrual periods, was identical with the pain experienced during the acute illness, differing only in extent and severity. While menstruation may usher in an acute attack of porphyria (Waldenström, 1937; Berg, 1945), we have not come across a case in the literature in which the acute attack was preceded by mild recurrent monthly attacks over so many years. The relation between menstruation and the underlying metabolic disorder is obscure.

Hypertension is said to occur often in acute porphyria (Waldenström, 1937; Denny-Brown and Sciarra, 1945)

*In recent work we have found that the extra porphyrin formed on heating the urine may be different in nature from the preformed uroporphyrin. (Gibson, Q. H., and Harrison, D. C. (1950) *Biochem. J.* In the press.)

With the onset of the abdominal symptoms the blood pressure is at first within normal limits, but it may rise gradually thereafter to reach levels that are definitely hypertensive. In our case there was no hypertension : the diastolic pressure varied between 60 and 70 mm. Hg, while the highest systolic pressure recorded was 135 mm. Hg. Leucocytosis, another frequent manifestation of acute attacks (Mason, Courville, and Ziskind, 1933), was also absent.

An interesting feature regarding this patient is her remarkable recovery following severe involvement of the nervous system. The extensive reviews of Mason *et al.* (1933) and of Waldenström (1937) indicate that the mortality rate in acute attacks is above 50%, and with neurological involvement the figure is much higher. Discombe and D'Silva (1945), however, described a case in which a man suffered an acute attack of porphyria with abdominal and neurological symptoms, which was followed by six relapses in three years. In spite of this the man recovered, and there was almost complete restoration of function in the paralysed muscles, though he continued to excrete uroporphyrin.

Mason *et al.* (1933) say that motor paralysis may develop rapidly or rather slowly, and they consider that recovery is not unusual in the more slowly progressive case. They do not, however, state precisely what they mean by these terms, and we therefore do not know into which group they would have placed our patient, the extension of whose neurological involvement occupied a total of seven days. In a case reported by Denny-Brown and Sciarra (1945), 16 days elapsed between the onset of motor weakness and its maximum severity. This patient slowly recovered from the attack, but died two years later, after a second attack with bulbar involvement.

The family history in the present case deserves comment. The current view is that acute porphyria is transmitted by a dominant gene which shows a small degree of penetrance. The absence of any manifestation of the disease in the members of the generation previous to that of the patient is not uncommon, but it was surprising to find on testing the urines of six members of this generation, including the mother and father, that there was no instance of the latent form of the disease, with urinary chromogens or porphyrins indicative of deranged pyrrole pigment metabolism. In cases in which the urine of both parents could be tested, Waldenström found only two instances in which neither parent showed any evidence of this abnormality.

Waldenström (1937) has shown the strikingly high incidence of acute porphyria in Scandinavia, suggesting a genetic background relatively favourable to the disease compared with that in England, for example, where the number of reported cases is very small. On the basis of past migratory tendencies from Scandinavia, Discombe (1948) suggested that cases of acute porphyria might be less rare in Scotland and Northern Ireland than in England. So far as we are aware, the present case is the first to be reported in Northern Ireland. On questioning, the parents stated that they knew of no Scandinavian link in their ancestry.

Until recently it was commonly believed that patients with acute porphyria excrete Type III uroporphyrin, in contrast to those with congenital porphyria, who excrete the Type I porphyrin. The work of Turner (1938) and of Watson, Schwartz, and Hawkinson (1945) threw doubt on this belief, and in the last few years several cases have been reported in which Type I porphyrin was excreted by patients with acute porphyria. Our patient falls into this category, and it is clear that the porphyrin type is not a diagnostic criterion for differentiating acute and congenital porphyria. A further implication is that in both diseases the porphyrin is likely to have arisen through an abnormality in the reactions involved in the building up of the pyrrole pigment rather than in those involved in pigment breakdown. Haemoglobin is made up of Type III pigment, and the degradation of this to a Type I porphyrin seems very unlikely.

As pointed out by Waldenström and others, the term "acute porphyria" is unfortunate, for it focuses attention on the acute episode of the disease and obscures the underlying chronic disorder of metabolism which exists between the severe attacks. The use of this term is understandable, of course, for the disease is rare, and physicians usually see the patient only in the acute attack, an attack which is often fatal.

In patients who recover, the warding off of further acute attacks is of paramount importance, since there is no known effective treatment for the acute episode. So far, all that can be done in this direction is to warn the patient of the danger of taking drugs which are known to produce porphyrinuria. Among those listed by Dobriner and Rhoads (1940) are barbiturates, sulphonamides, arsenicals, sulphonal, and alcohol. Barbiturates in particular have been mentioned by a number of workers as being potentially dangerous to these patients.

Summary

A case of acute porphyria is described in which a remission of two and a half years' duration has followed an acute attack with abdominal symptoms and severe paralysis.

The urine still contains porphyrin, which has been identified as uroporphyrin Type I. The urine of both parents and of all other relatives tested is free from porphyrin and its precursors.

We wish to thank Dr. S. B. Boyd Campbell for permission to publish details of this case, and Dr. C. L. Wilson for lending us the micromelting-point apparatus.

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The World Health Organization gradually expanded its activities during 1949, and in addition to its headquarters at Geneva has three regional offices in operation at New Delhi, for South-east Asia ; at Alexandria, for the Eastern Mediterranean ; and at Washington, for the American continent. Other regional offices will be opened to cover Europe, Africa, and the Western Pacific area. It also maintains field offices in China and Ethiopia, and an epidemiological intelligence station at Singapore. The total staff serving in the field and in offices is just under 400, representing 41 nationalities. At the end of 1949, 67 nations were members of WHO.

ACUTE IDIOPATHIC PORPHYRIA PRESENTING AS A PROGRESSIVE PARESIS OF LANDRY TYPE

BY

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[WITH PHOTOGRAVURE PLATE]

Cases of acute porphyria, although rare, are probably more common than is generally believed. The association of acute abdominal symptoms, neurological abnormalities, and port-wine-coloured urine is characteristic, but one or other of the members of the triad may be absent, and in such cases the diagnosis becomes very difficult. The findings at necropsy are slight and depend upon the application of special techniques, so that cases unsuspected during life are rarely recognized on the post-mortem table. It is only by constant awareness, both in the ward and in the laboratories, that such cases will be recognized. In view of these facts the following case history is worth recording.

Case Report

A housewife aged 45 was admitted to the Chelsea Hospital for Women under the care of Mr. Frank Cook on June 17, 1948, complaining of amenorrhoea. She stated that for the past two to three years her periods had been painful and had on occasion been preceded and followed by a brown vaginal discharge. Her periods had been regular until two months before admission, when she had missed a period; she had, however, begun to menstruate one week before admission. Her past history was uneventful except for an attack of appendicitis in 1938.

On examination a tumour the size of an eighteen-weeks-pregnant uterus was felt in the lower part of the abdomen. No other abnormality was detected in any system.

A diagnosis of endometriosis was made, and she was operated upon on June 18, subtotal hysterectomy and bilateral salpingo-oophorectomy being performed. At operation a chocolate cyst of the ovary was found, and it was noted that the small intestine was at one point adherent to the posterior surface of the uterus.

Her post-operative progress was good, though she required occasional sedation with barbiturates, until July 2, 15 days after the operation, when she complained of marked malaise and weakness. Physical examination revealed nothing abnormal. The urine was examined and found to contain a few pus cells and Gram-positive cocci. She was given sulphadiazine, receiving a total of 30 g. over the next few days.

On July 5 she complained of numbness of the thighs and buttocks. She was noted to be dull mentally. On examination retention with overflow was found, the bladder being distended up to the umbilicus; there was marked weakness of the legs; the deep reflexes in the legs and the abdominal reflexes were absent, and the plantar responses were flexor. At this time the blood urea was 44 mg. per 100 ml. and the haemoglobin 86%. The Wassermann reaction was negative.

By July 7 the weakness of the legs had increased and she complained of weakness of the arms. A lumbar puncture was performed, clear colourless fluid at normal pressure being obtained. The C.S.F. contained no cells, and Pandy's test for increased globulin was negative. By July 9 the patient had complete areflexia in all limbs, and objective weakness of the arms was noted. On July 10 the diaphragm movements became paradoxical. The patient was then transferred to the Westminster Hospital.

On admission she was found to be mentally confused, speech was slurred, and her respirations were very rapid. Examination of the C.N.S. revealed the following signs: no pupillary reaction to accommodation; bilateral absence of corneal reflexes; left lower facial paralysis; a flaccid tetraparesis, most severe in the legs; weakness of the trunk muscles; complete absence of all deep reflexes; absent abdominal reflexes; and ill-defined areas of anaesthesia over both legs. Urine was sent to the laboratory for examination, as it was thought to be infected. *Streptococcus faecalis* was cultured. A specimen was sent to the Chemical Pathology Department: it was reported on as follows: "Urine almost normal in colour, but darkened on heating. Waldenström's test for porphobilinogen strongly positive. Total porphyrin 25 mg. per litre The porphyrin was mainly ether-insoluble (uroporphyrin). Insufficient material for further identification."

On July 11 the patient was noted to be more dyspnoeic. the C.N.S. signs were unchanged, but examination of the chest revealed a poor air entry and scattered rales. A double-exposure *x*-ray film of the chest showed paradoxical movements of the diaphragm right and left. At 5 p.m. her respirations suddenly rose to 41 a minute and she died.

Post-mortem Examination.—This was performed by Dr. J. G. Humble on the day after death. Examination showed a curious purple-brown coloration of the heart muscle. Black pigment was scattered over the peritoneum. The trachea and large bronchi were full of mucopus, and bilateral basal pulmonary oedema was found. The brain and spinal cord appeared congested, and there was a definite pressure cone. The right sciatic nerve seemed oedematous.

Microscopical Examination.—Sections of the right sciatic nerve stained with haematoxylin and eosin (Plate, Fig. 1) showed patches of lymphocytic infiltration, congestion of vessels, and perivascular collections of polymorphonuclear leucocytes and mononuclear cells. Sections of the lumbar and cervical cord stained with haematoxylin and eosin and with toluidine blue (Fig. 2) exhibited degenerative changes in the anterior horn cells, many of which showed central chromatolysis, some being reduced to mere ghosts. Sections of the cerebellar cortex showed severe degenerative changes in the Purkinje cells. Sections of the midbrain, basal ganglia, and cerebral cortex failed to reveal any abnormalities with the two staining methods used.

Comments

This woman had no relevant past history. At no time previously had she reacted adversely to any drug; the only drugs given after operation were potassium citrate, sulphadiazine, and an occasional dose of phenobarbitone. Her illness apparently lasted, from first to last, only 10 days. The spread of symptoms and signs was from below up (Landry type). A double-exposure *x*-ray film taken the day she died showed paradoxical movements of both sides of the diaphragm and a small area of collapse in the right lower lobe. Had not examination of the urine revealed uroporphyrin the diagnosis might have been completely missed, even at necropsy. The triad of abdominal symptoms, neurological signs, and highly coloured urine so suggestive of porphyria may not always be present; only one or two of these findings may be forthcoming, as in this case.

The peculiar clouding of consciousness and confusion noted in our patient have often been observed before—for example, Case 2 of Mason *et al.* (1933), and Abrahams *et al.* (1947). The ascending (Landry) type of paralysis has been known to occur in acute porphyria for many years (Courville and Mason, 1931; Kinnear Wilson, 1940). Occasionally there may be a recovery from an acute attack, with death in a second acute attack (Denny-Brown and Sciarra, 1945; Davies, 1949).

The microscopical lesions in the C.N.S. are those that have been described by previous writers (Denny-Brown and Sciarra; Mason *et al.*). With the exception of the changes

in the Purkinje cells, they fit well with the clinical signs and provide an explanation for the respiratory failure which was the immediate cause of the patient's death.

It is impossible to be certain whether this case should be regarded as one of acute idiopathic porphyria or whether it was toxic in origin, as we were unable to obtain enough urine for the porphyrin to be typed. Of the drugs which she received, the sulphadiazine would have been the most likely cause of her condition; Dobriner and Rhoads (1940) mention both clinical and experimental evidence that sulphonamides may cause increased excretion of porphyrins, and sulphadimidine (sulphamezathine) was one of the drugs administered in the fatal case reported by Abrahams *et al.* The difficulty remains that in all reported cases of toxic porphyria the predominant excretion product has been coproporphyrin.

In our case symptoms, though slight at first, preceded sulphadiazine administration. The balance of evidence therefore seems to us to be in favour of this being an acute idiopathic porphyria rather than a toxic one. The urinary findings and the rapidly progressive neurological picture would also make this the more likely diagnosis.

Our thanks are due to Professor R. J. V. Pulvertaft and Professor N. F. Maclagan for help and criticism; and to Dr. P. Hansell, of the Department of Medical Photography, for the photomicrographs.

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CONVULSIONS IN CHILDHOOD

BY

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The article by Nathan and Ransford (1949) prompts me to record six cases of convulsions in children between the ages of 5 and 11 years. These were observed between 18 and 25 years ago and their subsequent medical history has been recorded. I attended the mothers of Cases 4, 5, and 6 at their confinements. The observations were made during an investigation of the cortico-thalamic reactions to visceral tensions, which may represent only a small group of a type of epileptic convulsion—the viscero-cortical. The neurological syndrome, however, with which these cases appear to be associated has since become the basis of certain obstetrical procedures. These observations were made before electroencephalography came into use, and there was then no knowledge of cortical electrical potentials and the variations of their rhythmical patterns.

Case 1

A boy aged 10 suddenly and for no apparent reason fell to the floor in a typical epileptic fit The fits recurred every 15 minutes for an hour and lasted two to three minutes. He had bitten his tongue and become incontinent. When I saw him he had just recovered from a fit, was lying on a bed, restless, unconscious, but frowning and mouthing his lips over closed teeth as if trying to free them of an unpleasant taste. There was no history of constipation. He was not cutting any teeth. He had had a large tea—it being Christmas Day. A few minutes after the fit he became conscious and I decided to empty his stomach. This was effectively done. The resulting vomit was enormous. After an hour's rest he was perfectly normal and had no memory of what had happened, except that he had been sick.

He is now 35 years of age, has never had a recurrence of these attacks, was an exceptionally brilliant student at school, and was an outstanding athlete. He is a member of a family whose names are well known in the athletic and industrial world.

Case 2.

A boy aged 6 had a series of epileptic fits for no apparent reason. They occurred every five minutes and had been going on for over an hour when I saw him. He was well nourished and a good specimen of a curly-haired boy. His history was that he had not felt well that day. He was lying on the bed in a fit when I saw him, with his head thrown back, his back hollowed, his legs rigid, and his arms in tonic spasm extended in front of his abdomen. His breathing was stertorous, his face cyanosed, his teeth tightly clenched, and strabismus showed through widely opened eyelids. There followed a series of clonic contractions from which he relaxed with a groan. He had not bitten his tongue, but there was the puckered frown upon his forehead and mouthing similar to Case 1. Not having felt well, he had had only a few mouthfuls of bread and milk during the day. There were no history of injury, no pyrexia, and no evidence of the onset of an acute inflammatory condition.

Examination of the abdomen however, revealed a distended descending colon and sigmoid lying like a large rope stretching almost from the splenic area to the pelvis. He was at once given a rectal injection of 2½ oz. (70 ml.) of equal parts of glycerin and oil. A mass of scybala and constipated faeces was passed, being followed after a few moments by a large and well-formed evacuation of the bowel which in mass was out of all proportion to the size of the child.

This fine boy was killed in action as an officer of the Guards Brigade at the age of 25. He had never had any recurrence of his convulsion, but had grown up a scholar and athlete. His father had been an athlete of considerable accomplishment.

Case 3

A boy aged 11 was sent into hospital with a history that he had epileptic fits. His doctor had never known him to be ill previously. He came of a good artisan stock and had several brothers and sisters. There was no history of illness in the family, epilepsy or allergy. Twenty-four hours before admission to hospital he had his first fit, which was followed by one approximately every hour. When he was admitted he was unconscious. His temperature was over 100° F. (37.8° C.) and he was considered to be suffering from acute infective encephalitis.

When I first saw him he was lying unconscious in bed with his head thrown back. A gentle effort to bring it forward precipitated a fit which lasted about two minutes. When the clonic movements ceased he lay frowning and mouthing as did the two previous cases.

Sir Henry Head pointed out to me, when I was his house-physician, that if convulsions were accompanied by mouthing a "visceral accompaniment" should be suspected. Between attacks this boy had complained of acute abdominal pain and put his hands over the lower abdomen. He lay fully stretched out upon the bed. Abdominal examination revealed a firm lump, apparently in his caecum. There was no tenderness or peritonism. His white cell count showed an eosinophilia with no rise of polymorphonuclear leucocytes. Assuming from these observations that his might be a case of ascaris toxaemia with visceral irritation, I gave him santonin followed by castor oil, which he was able to swallow. I refrained from doing an immediate lumbar puncture. Eight hours later he was sitting up in bed looking perfectly well, having no memory of what had happened. A jar was produced containing four large roundworms. In 24 hours the treatment was repeated and another bunch of large roundworms was expelled. At the end of three days he was sent home perfectly well.

He grew into a fine athlete and spent many years as a successful professional footballer. He was 29 when I last heard of him, about four years ago, and had never had a day's illness. I understand that his father had also been a good athlete.

Case 4

This case, that of a boy aged 6, was more difficult because it was complicated by the possibility of injury. He was riding a "fairy" cycle down a macadam road when he shot over the handlebars and landed on his forehead. He got up almost immediately and, although dazed, did not lose consciousness. He was taken home and I saw him within ten minutes. There was a very large swelling, apparently a haematoma, on his forehead, about 3½ in. (8.8 cm.) in diameter, protruding nearly 1 in. (2.5 cm.) from the frontal bone. A radiograph did not reveal a crack, depression, or fracture of the frontal bone. The injury was severe enough, however, to warrant careful treatment.

He was kept in bed and quiet in order that the swelling might subside. All went well for six days, when the necessity for this treatment was questioned by his parents. It was insisted, however, that no head injury should be taken lightly. On the evening of the sixth day I was summoned urgently because the boy was looking strange. Fortunately I was again able to be at the house in a few minutes, to learn that he had just had an epileptic fit. When I saw him he was in a drowsy condition and my efforts to examine him resulted in a second convulsion which was typically epileptic. There was nothing to suggest that it was Jacksonian in type. After a tonic phase there was a general convulsion which lasted well over a minute. It was very severe. His breathing was stertorous, he was cyanosed, and when he relaxed the mouthing that has been previously described was noted. There was no puckering of the forehead, however, because it was too swollen and tender.

In this case there was obviously more than one consideration. From the nature of the convulsion visceral influence appeared to be likely, but leaking subdural haematoma had to be taken into consideration. His bowels had not been open for 48 hours. On examining his abdomen a large palpable colon was found in the left iliac fossa. An injection of glycerin and olive oil was again resorted to. There was a copious movement of the bowels, followed 20 minutes later by a second evacuation quite abnormal in size. In a short time the boy became clear in his mind. He looked about him as a child looks around when wakened by light at night—at first a little dazed and then completely comprehensive. He called me by my name and asked why I was there. He never had a recurrence of this condition. He grew to be a good athlete with an exceptionally alert mind. He was killed while a pilot in the Royal Air Force at the age of 22. This boy's father was one of the greatest lawn tennis players of all time.

Case 5

I was asked to see a boy aged 5 because he was not feeling well. His symptoms were quite indefinite. He was by nature an extremely cheerful and sturdy boy. When I saw him he was sitting on his nurse's knee, which for him was quite unusual.

I went into the night nursery while he was being put to bed, with the idea of observing his behaviour and talking to him before examining him, when without any warning he suddenly became rigid, with his head flung back and his back arched, and he would have fallen to the ground if his mother had not caught him. He had a series of clonic movements of the arms and legs; his eyes were open, and there was strabismus and rigid opisthotonos. After about a minute, which seemed a very long time, the clonic movements ceased; he became relaxed and lay still on the bed with his fingers working in the palms of his hands and his mouth moving in the typical manner previously described. Two or three minutes later he was violently sick. He brought up his lunch and his tea, neither of which appeared to have been digested.

This boy had a congenital pyloric stenosis, for which Rammstedt's operation was performed when he was 5 weeks old. He grew up to be a normal intelligent boy and an outstanding athlete. He did not suffer from any illness or from any recurrence of convulsions. He is now about 24 years of age. His father was an all-round athlete of recognized ability, both at the university and afterwards, whose books are read in many countries.

Case 6

This patient was a girl aged 9, a heavily built sturdy child. She was staying in my house. Half an hour before breakfast she was playing happily in the nursery, feeling quite well, when without any warning she fell flat on the floor. I was with her almost immediately and found her lying with her eyelids open and her teeth clenched. There were strabismus, clonic movements of arms and legs, and deep stertorous breathing. The convulsion lasted an alarming time: it was the most prolonged that I have ever witnessed, probably three minutes before she relaxed. She remained unconscious. After a few minutes she was violently sick, having had nothing to eat that morning. I carried her to her bed and she vomited a second

Tabulated Record of Cases

	Past and Family History	Gastro-intestinal State at Time of Attack	No. of Fits	Fall	Type of Convulsion	Incontinence of Urine	Time Unconscious	Mouthing and Frowning Between or After Fits		Treatment	Result	After-Result	1949
								Mouthing	Frowning				
Case 1: Boy, 10 years	No epilepsy. No protein-sensitive diseases	Overloaded stomach	3 or 4 in an hour	Yes	Tonic spasm; opisthotonos; clonic movements; relaxation	Yes	2½–3 hours	Yes	Yes	Emptied stomach	Complete recovery very few hours	Excellent physical and mental development. No recurrence of fits	Aged 35
Case 2: Boy, 6 years	,,	Overloaded rectum	10 or 12	Lying down at onset	,,	,,	1–1½ hours	,,	,,	Emptied rectum	,,	,,	Killed in action, aged 25
Case 3: Boy, 11 years	,,	Mass of intestinal parasites (roundworms)	Between 20 and 30	No history	,,	Yes and faeces	36 hours approx.	,,	,,	Expelled parasites	,,	,,	Aged 35
Case 4: Boy, 6 years	,,	Overloaded rectum	2	Lying down at onset	,,	Yes	10–15 minutes	,,	No	Emptied rectum	,,	,,	Killed flying in R.A.F., aged 22
Case 5: Boy, 5 years	,,	Overloaded stomach with delayed digestion	1	Yes	,,	,,	1–2 minutes	,,	Yes	Emptied stomach	,,	,,	Aged 24
Case 6: Girl, 9 years	,,	,,	1	,,	,,	No	3 or 4 hours	,,	,,	,,	,,	,,	Aged 25

time. Both these vomits were copious: I estimated that the two of them were nearly four pints (2.27 litres) of stomach content. The food was undigested, her lunch and tea of the previous day being recognized.

She remained in a comatose state for approximately four hours and during that time the same frowning and mouthing was observed. When she regained consciousness she complained of headache. There was no previous history of any similar attacks, or any family history of convulsions or allergy, and she was not at the time cutting her 10-year molars.

She has grown into a strong healthy woman, weighing nearly 12 stone (76.2 kg.), though not excessively fat. She has had a fine athletic career and obtained the maximum credits in her School Certificate. She comes of a family who have combined fame in politics and science with considerable athletic distinction.

Discussion

In each case a short note on the family and stock from which these children came has been appended. The similarity of types is not without interest. A high degree of physical and mental efficiency and personal achievement is common to them all. Is there, therefore, any association between these factors and predisposition to cortical storms of this nature?

The similarity of many features of the tabulated record of these cases suggests that a certain type of convulsion, whether recurrent or not, may be initiated by visceral tensions, irritations, and spasms. In children whose thalamic function is highly sensitized to sensory stimulus a visceral sympathetic assault may disturb integration of the normal thalamo-cortical relationship. Instead of protective, balanced motor responses an extensive cortical storm is precipitated by uncontrolled neural discharges, either causing or resulting from paroxysmal cerebral dysrhythmia. The integrity of the cortical response depends upon the intensity of tension or irritation, to sensitivity of the visceral nerve endings, the conductivity of the sensory neurones, and the quality of the thalamic receptivity. Abnormality of any one of these factors may predispose to convulsions. Later observations have shown that clinical manifestations of visceral tension result in variations of cortical discharge compatible with this theory. It has been possible to observe this during childbirth, and a large number of cases have provided evidence that the prevention and treatment of visceral tension greater than the normal mean may preserve the integrity of the viscero-thalamo-cortical syndrome.

In the course of the years I have recorded three cases of sudden epileptic fits during the late first stage of labour. None of these women showed any signs of toxaemia. There was no raised blood pressure and no albuminuria or excess of acetone in the urine. All three were primiparae. Two, however, had suffered from attacks of petit mal and the third had spent some months in a home with a severe nervous breakdown. All three were highly emotional—a state which results in resistance by the circular muscles of the uterus to the dilatation of the cervix. This in effect is the contraction of two opposing groups of muscles at the same time, giving rise to abnormal tension.

The explanation of these fits, which had no relation to eclampsia, was that excessive tension in the lower uterine segment overloaded the hypersensitive afferent sympathetic fibres from that area of the uterus. The thalamic receptors were already disturbed by emotional imbalance, with the result that a convulsion or cortical storm was precipitated by uncontrolled neural discharges. It is significant that all three remained well during the second stage of labour, when, in the absence of abnormality, there is relaxation of the lower uterine segment.

The possible relationship of this syndrome to certain types of convulsion in pregnancy and labour cannot be overlooked, and it seems reasonable to suggest that a high percentage of the non-recurrent epileptic fits in children may be explained upon this hypothesis.

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ENDOTHELIOMA OF THE PLEURA

REPORT OF A CASE

BY

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[WITH PHOTOGRAVURE PLATE]

Since the original account by Wagner (1870) there has been much argument about the pathological entity of endothelioma of the pleura. Some pathologists (Robertson, 1924) denied its existence. There does seem, however, to be a small group of cases (Klemperer and Rabin, 1931), comprising about 0.2% of all necropsies (Saccone and Coblenz, 1943), in which such a diagnosis must be made. The clinical picture is fairly constant, the main features being increasing dyspnoea and pain in the chest associated with great thickening of the pleura and massive pleural effusion (Banyai and Grill, 1933). The reason for reporting this case is that the clinical and radiological signs were unusual and the diagnosis unexpected.

Case Report

The patient, a married woman aged 41, was first seen by one of us (A. W.) on November 24, 1947, when she complained of lassitude, dry cough, and low-grade fever of one month's duration. She was born in Germany and had lived there and in North-west Europe until her arrival in this country just after the war. There were no significant facts in her past or family history. On examination she looked well, was adequately nourished, and no abnormal physical signs were found. Radiographs of the chest showed two rounded homogeneous shadows on the left side, one large and one small, with, in the lateral view, two more small shadows lying anteriorly (Plate, Fig. 1).

These appearances suggested multiple hydatid cysts or metastases possibly from a hypernephroma. On December 12 she was admitted to the Middlesex Hospital for investigation, and on further interrogation she denied contact with dogs. She now complained of vague pain in the left chest, and there was some note impairment over the left upper chest anteriorly. No evidence of a primary growth was found in the thyroid, breast or pelvis. The temperature varied between 99 and 100° F. (37.2 and 37.8° C.), the pulse between 80 and 100, and the respirations remained at 20; the white cells numbered 8,000 (neutrophils 74%, lymphocytes 18%, monocytes 7%, eosinophils 1%); stomach washings for tubercle bacilli were negative; the Mantoux test was positive at 1 in 1,000; the Wassermann reaction and Casoni and hydatid complement-fixation tests were negative; and an intravenous pyelogram was normal. An artificial pneumothorax showed that the tumours were attached to the parietal and visceral pleurae.

On January 21, 1948, Mr. T. Holmes Sellors performed a thoracotomy, at which many rounded pinkish tumours varying

in size from a pinhead to 3 in. (7.6 cm.) in diameter were found. They were attached to the parietal and visceral pleurae, those on the visceral pleura extending into but not invading the lung. The four largest tumours were removed by diathermy and on section were seen to be very vascular and well encapsulated.

Histologically the tumours were composed of spindle-shaped cells, in places showing a whorled arrangement and in other areas apparently lining clefts (Fig. 2). At Professor Scarff's suggestion the sections were examined by a consultant panel of pathologists, whose opinion favoured the diagnosis of endothelioma.

Convalescence was uncomplicated except for the development of a complete palsy of the left vocal cord. The fever disappeared and only a small pleural effusion formed; this was soon absorbed. The patient left hospital on January 16. On May 6 she felt well, but complained of a dry cough, slight dyspnoea, and aching pain over the left lower chest. There was some note impairment over the left base, with weak breath sounds, and radiography revealed a number of rounded shadows on the left side, particularly at the left base. On July 17 she was readmitted. She was now very ill with fever, dry cough, and severe dyspnoea. The signs were little changed, and a radiograph showed a further increase in the size of the tumours and possibly some fluid in the left pleura, but no fluid was found on paracentesis. She was seen by Professor Windeyer, who agreed to give deep *x*-ray therapy, although it was realized that the growth was likely to be radio-insensitive. Owing to deterioration of her general condition this treatment was stopped after two applications. A fortnight before her death on August 15 she developed albuminuria and gross oedema of the trunk and legs.

Necropsy. (Extract from Bland-Sutton Institute Post-mortem Report.)—The left pleura was studded with multiple nodular growths up to 2½ in. (6.35 cm.) in diameter, arising from both visceral and parietal layers, the larger ones showing central softening. The tumours had a firm grey surface on section. Those arising from the parietal pleura were polypoid and those from the visceral surface indented the lung without actual invasion. The tumours were most numerous at the base anteriorly. There was no evidence of growth in any of the bronchi or general thickening of the pleura. One gland at the bifurcation of the trachea was involved by growth. The right pleural sac contained 30 oz. (852 ml.) of clear fluid and the right lung was oedematous, but there was no growth in pleura or lung. The liver and kidneys showed amyloid change. No primary growth was found in any other organ and, apart from the one lymph node, there were no metastases.

Histology.—Sections of the growth showed spheroidal eosinophil epithelioid cells with vesicular nuclei. In places there were attempts at tubule formation; elsewhere the cells were arranged in whorls. The lymph node was invaded by the growth.

Discussion

The usual features of endothelioma of the pleura are an increasing dyspnoea, generalized thickening of the pleura, which may be detected on paracentesis, and sero-sanguineous pleural effusion, which appears early and becomes massive. Pain in the chest is often severe and persistent, and is unrelieved by withdrawal of fluid. There may be areas of anaesthesia on the chest wall (Barrett and Elkington, 1938). Metastases are infrequent and tend to appear late in the disease (Evans *et al.*, 1946). Death usually occurs in about nine months, but may be postponed for two years.

This case was in some ways unusual. Pain in the chest was at no time severe, although some discomfort was present in the last weeks of life. Generalized pleural thickening was absent and pleural effusion appeared only transiently after thoracotomy. The initial radiological changes suggested metastatic deposits rather than a primary growth of the pleura. However, the course of the illness was characteristic, as was the basal location of the majority of the tumours, which did not invade the neighbouring structures (Weissman, 1946). Only one metastasis, in the local lymph node, was discovered, and in spite of careful search no other primary growth was detected. Final support for the diagnosis of endothelioma of the pleura was given by the histological picture.

This case proved an interesting problem in diagnosis. Owing to the atypical features, particularly the absence of effusion, endothelioma of the pleura was unsuspected until thoracotomy.

Once this diagnosis has been made, the patient is saved much profitless investigation, but, apart from symptomatic measures, little can be done to ameliorate the condition.

Our thanks are due to Dr. H. K. Graham Hodgson for the radiograph, to Professor R. W. Scarff for the pathological work, and to Dr. A. C. Thackray for the photomicrograph.

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FRACTURE OF THE FIRST RIB

ITS OCCURRENCE AND CLINICAL DIAGNOSIS

BY

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[WITH PHOTOGRAVURE PLATE]

Fractures of the first rib, although not unknown at the end of the last century (Lane, 1885), have been regarded as comparative rarities, and reference to them is rather scanty up to about 1944–5, since when a few articles have appeared discussing the occurrence, the aetiology, and even the very existence of the condition. For these various opinions one would do well to consult the original articles by Aitken and Lincoln (1939), Etter (1944), Alderson (1944, 1945, 1947), Blair Hartley (1945), and Bowie and Jacobson (1945). It is sufficient to say at present that a fracture of the first rib is a clinical entity, and that it can be an extremely acute and painful injury, just like any other fracture. It is becoming more widely recognized, probably owing to the increasing use of mass miniature radiography and routine chest investigations by the Services and other authorities.

In 1944 Alderson reported 35 cases of anomaly of the first rib in 55,451 routine chest examinations in Royal Naval personnel. He noticed that the lesion occurred in various forms proximal to the scalene tubercle, appearing in some cases as partial or complete, transverse or oblique fissures, whilst in others it either took the form of a fusiform swelling of the bone (callus formation) or, as in a few cases, appeared like a pseudo-arthrosis. All his cases were males, even though 3,433 women were examined, and the highest incidence occurred between 15 and 20 years of age. Of the 35 cases, five had a history—two of local trauma and one of pain after carrying heavy materials. He regarded the condition as a stress fracture occurring

gradually in the majority of cases, often in relation to muscular violence. Later, in 1947, he reported a detailed radiological series of 73 cases, and these he classified as (*a*) spontaneous symptomatic, (*b*) spontaneous asymptomatic, (*c*) fracture due to muscular stress, and (*d*) fracture associated with trauma.

Some correspondence took place in the journals about the condition, and Blair Hartley, while disagreeing with Alderson on some principles, agreed that the condition was more common than had been accepted in the past, occurring often without enough symptoms to warrant a clinical or radiological examination. Hartley considers some of the cases to be "fatigue" fractures, but these, he states, are not related to muscle pull nor are they resultant from muscular action; they are essentially incomplete. On the other hand, the "fracture can occur where the bone is completely severed. Here there is frequently quite considerable displacement of the fragments," non-union or the formation of a false joint having also been noticed in some cases. According to Hartley there is abundant evidence that muscle pull does precipitate this type, and in a number of cases no other cause could afford a reasonable explanation.

Both Alderson and Hartley are agreed that lifting heavy weights is one of the occupations most likely to produce fracture of the first rib.

It is not my object to enter the field of argument as regards the aetiology of the condition, but it would be as well to mention some of the explanations put forward to account for the occurrence of the fracture. It will be remembered that the scalenus anterior and medius are inserted on each side of the subclavian groove, and it was stated in the *Lancet* (1945) that if these two muscles were to contract suddenly the subclavian artery and the lower trunk of the brachial plexus could act as a "restrainer," holding down the intervening portion of the rib at the fracture site, which is so constant in position.

It has been suggested that the powerful serratus anterior (first digitation) and the subclavius could also play a part, and this may be the mechanism in the cases in the present series in which forcible elevation of the arm was known to have taken place. Trauma transmitted through the clavicle and sternum has also been quoted as a probable cause of the fracture, and, again, in the present series there is a case in which fracture occurred after the patient had collided shoulder to shoulder with a goalkeeper. The presence of other radiological lesions, congenital or otherwise (tuberculous osteitis of ribs, congenital deformities of the ribs, or the presence of lung disease), may perhaps have some significance in those cases in which such lesions have occurred, although this is highly hypothetical.

The present series of 25 cases, all males, are, with one exception, those that have been diagnosed in Army personnel, and have been seen within a period of about nine months. Some were noticed as abnormal on mass-miniature radiography and were followed up by full-size chest films; others were noticed on routine chest investigation; and the remainder presented themselves as acute chest or shoulder injuries. In these acute cases the symptoms and signs were of an extremely severe but characteristic nature, and the clinical picture, when once seen, could not easily be forgotten. The majority of cases no doubt occur with minimal signs and symptoms, and in civilian practice these patients would perhaps not have bothered their doctor, thinking the pain in their shoulder to be due to "rheumatism" or a sprain, as it is usual for all pain to disappear in four or five days. The condition is certainly not so uncommon as was believed—at present two or three cases a month, mostly in the healing form, are seen at this hospital.

As a guide to the clinical diagnosis of the severe form two case histories of such patients are quoted in detail.

Case 1

Craftsman A., aged 18, was seen on March 10, 1949, with a history that his right arm had been forcibly hyperabducted suddenly while playing with some of his friends. They all heard a terrifying click. When seen he was supporting his right arm in the manner of a patient with a dislocated shoulder and complaining of severe pain, located vaguely "under the shoulder-blade," when he attempted any movement of the arm, and also of some shooting pain radiating from the axillary region down the inner side of his arm to a distance of about 3 in. (7.6 cm.) below the elbow-joint.

On examination the outline of the shoulder appeared normal, but any attempt at movement caused excruciating pain in the scapular region. Passive abduction with or without external rotation was bearable to 90 degrees, but was associated with a loud clicking noise. There was no localized tenderness of the shoulder region, but deep inspiration and compression of the upper ribs was accompanied by the same severe pain. Power of the affected arm was greatly diminished on testing the patient's grip and his ability to act against resistance. *X*-ray examination revealed a complete fracture of the first rib at the level of the scalene tubercle, but there was no displacement (Plate, Fig. 1).

The arm was immobilized in a collar-and-cuff for one week, and when the patient was seen a week later he complained that there was still some pain and that the clicking noise could still be heard. This clicking disappeared at the end of the third week, by which time the pain had practically gone, abduction was full, and he was able to carry on with normal duties. A radiograph showed that callus was beginning to form. At the sixth week he complained of a "flare-up" of the pain, which gradually disappeared until he was free from symptoms.

Case 2

Pte. B., aged 18, complained of severe pain in his right shoulder following a fall out of a window on to his outstretched right arm while practising ju-jitsu three days previously. The onset of pain was gradual, starting as an ache around his shoulder-blade on the second day and increasing greatly in severity on the third day.

On examination (on the third day after the accident) the outline of the shoulder was normal. Abduction of the shoulder to 90 degrees was possible without much discomfort, but above this the patient had an excruciating pain which was located "behind the shoulder-blade"; there was no localized tenderness, but compression of the upper ribs with deep inspiration was accompanied by pain. There was no localized tenderness on deep palpation of the supraclavicular fossa, although compression of the clavicle, with the thumb of the examining hand over the scapula and the other fingers on the hand placed over the clavicle, caused severe pain. Power in the arm was greatly diminished.

A radiograph (Fig. 2) showed a complete fissure in the region of the scalene tubercle, with marked widening of the fissure on the medial aspect of the rib, giving the appearance of an oblique fissure line. The arm was immobilized in a collar-and-cuff for two weeks, and when seen two weeks later the patient stated that all his symptoms had disappeared in about ten days. On examination all shoulder movements were normal and painless. A radiograph did not show any callus formation, but this appeared to be forming slowly at the sixth week.

Discussion

The pain on active abduction, especially over 90 degrees, pain on deep inspiration, together with a feeling that it was under the shoulder-blade, and also some weakness in the grip of the affected arm, are characteristic of the fracture when it presents as the acute form. However, the milder

cases often present with no physical signs and have very minor symptoms; as an example of this the following case is quoted.

This particular patient (Case 9) was a miner, and six months previously he had noticed the onset of "rheumatic pains" in his left shoulder after he had lifted a particularly heavy weight. The pain came on gradually but increased in severity until it forced him to lose half a shift that day; he also had some clicking in his shoulder for three days. The symptoms gradually subsided and within ten days he felt perfectly normal. He did not bother to see a doctor at the time, because he paid no importance to his symptoms; he has had no trouble with his shoulder since. Routine mass miniature *x*-ray examination showed an old fracture of the first left rib with massive callus formation, the fissure line being still faintly present.

Details of the 25 case histories presented in this series are set out in the accompanying Table, together with a synopsis of the radiologist's report (Major McKelvie, specialist in radiology, R.A.M.C.). The fracture occurred with about equal frequency on either side (13 on the right side and 11 on the left side, together with one bilateral case), the majority being in youths between the ages of 18 and 19; only five were over 19. Of the 25 cases, three had other radiological lesions—two had vestigial first ribs on the other side and one had absence of the transverse process of the first thoracic vertebra on the same side as the lesion. The radiological picture is remarkably constant as regards the site of the fracture, and the lesion appears in one of the following ways: (1) the "type" in which a fissure line is present with marked widening of the fissure line on the medial aspect of the rib; (2) the complete fracture with no displacement of the fractured ends; (3) an old fracture with minimal callus formation, appearing very much like a pseudo-arthrosis (Fig. 4); and (4) the type in which callus is well formed, appearing as a buttress formation (Fig. 3) in the region of the scalene tubercle, and in which the fissure line may or may not be still present.

In view of the position of the fracture and the constancy of its site the question of involvement of the brachial plexus and subclavian vessels would arise. The callus, though slow in formation, is often of considerable size, but in this series no obvious lesion of these important structures could be demonstrated clinically. Only one patient (Case 1) complained of pain which might have suggested damage to the brachial plexus. In this case the pain radiated from the roof of the axilla down the medial aspect of the arm to a few inches below the elbow-joint. There was no

Analysis of Cases

Case No.	Age	Side	History	Radiological Findings
1	18	Right	Right arm forced upwards violently; loud click heard. Very severe symptoms. Marked clinical signs	Complete transverse fissure of first right rib at level of scalene tubercle. No displacement, otherwise radiograph normal. Follow-up radiographs show callus forming
2	18	,,	Fell out of window on to outstretched right arm; severe symptoms and marked clinical signs	Complete fissure of first right rib in region of scalene tubercle, with widening out of fissure line medially. No other lesion seen: follow-up radiograph shows callus formation
3	18	Left	No past history on interrogation and no physical signs; M.M.R. case	Old healed first rib fracture in region of scalene tubercle showing buttressing callus formation. Otherwise normal
4	19	,,	No history. M.M.R. case	Old healed first rib fracture at level of scalene tubercle showing buttressing formation. Otherwise normal
5	19	,,	History of some pain in left shoulder. No detailed record of signs and symptoms	Complete fissure of first rib in region of scalene tubercle. No other abnormality
6	26	Right	After lifting 2 loads each of 100 lb. (45·36 kg.) had aching in right shoulder-blade region, which increased in severity and was severe for 4 days. Pain on abduction. Marked physical signs	Complete fissure of first right rib at region of scalene tubercle. Follow-up radiographs
7	18	,,	Routine radiograph of chest	Old fracture of first rib in region of scalene tubercle. Not healed: some callus present, but irregular fissure still marked. Vestigial first rib present on left side
8	18	,,	No history or signs. M.M.R. case	Old fracture of first rib in region of scalene tubercle. Complete fissure still present. Ununited. Appearance suggestive of pseudo-arthrosis
9	20	Left	Remembers having "rheumatics" in shoulder six months previously after lifting a heavy weight at a colliery. Lost half a shift but did not bother doctor. M.M.R. finding	Healing fracture of first rib in region of scalene tubercle. Complete, but no displacement
10	18	Right	History of trauma to shoulder a few months previously; still tender in shoulder region at times. Swelling palpable in supraclavicular fossa. M.M.R. findings	Healing fracture of first rib in region of scalene tubercle. Callus present but fissure visible
11		,,	?	Massive buttressing in region of right scalene tubercle, but fissure still present. No other abnormality seen
12	19	,,	Routine chest investigation	Ununited old first rib fracture in region of scalene tubercle. Fissure still present. Picture suggestive of pseudo-arthrosis
13	18	Left	Does not remember any pain whatsoever at any time in his shoulder. Was a tin-worker and accustomed to carrying heavy weights. M.M.R findings	Thin narrow first rib with fissure in scalene tubercle region. There is absence of the transverse process of the first thoracic vertebra on the same side
14		Right	History of pain lifting heavy weights. Minimal symptoms some time ago. Routine chest examination	Old healing fracture of first right rib in region of scalene tubercle. No other abnormality detected
15	18	Left	?	Old ununited fracture of first left rib in region of scalene tubercle. Callus present, but wide fissure between bone surfaces resembling pseudo-arthrosis
16	19	,,	No history	Healed fractured first left rib in region of scalene tubercle. Callus and buttressing present
17	19	,,	Past history of coughing and chest pains. No significant occasion to account for *x*-ray appearance	Healing fractured first rib in region of scalene tubercle. Callus present. Heavy lung markings
18	18	,,	When playing football crashed into goalkeeper shoulder to shoulder. Followed by onset of fairly severe pain on inspiration and movement of arm. Symptoms lasted 10 days	Fissure of first rib in scalene tubercle region with marked widening of fissure line at medial margin. No other lesion. Follow-up radiographs show callus formation
19	20	Right	History of "pleurisy" 5 months ago. Pain went off after 1 week. No symptoms since. Routine radiograph	Old fracture of first right rib. Callus present. Buttress appearance. Fissure line present
20	18	,,	History of onset of pain after lifting heavy weight in coal-mine. Marked symptoms and clinical signs	Recent fracture of first rib in scalene tubercle region with widening of fissure line on medial side. Follow-up radiographs show callus forming
21	18	Left	History of spraining left shoulder few months previously, lifting a heavy mattress at home. Pain lasted 3 days and was of slight severity. No symptoms or pain since. M.M.R. findings	Old fracture of first left rib. Massive callus formation, but faint fissure still present. No other abnormality
22	26	Right	Remembers slight pain in right shoulder for 4–5 days after lifting heavy oil-drums about six months previously	Healing fracture of first rib in scalene tubercle region. Complete fissure still present, but callus forming
23	35	,,	Routine chest examination for welder. No history	Healing fracture of first rib in scalene tubercle region. Callus forming. Fissure line complete. Also vestigial first left rib present. Heavy vascular markings
24	18	Left	M.M.R. No history	Healing fracture of first left rib. No other abnormality
25	18	Right and left	No history to give. No physical signs or symptoms. M.M.R. findings	Bilateral fractures of first right and first left ribs. Callus forming. Buttress appearance. Fissure lines present

alteration of sensation, tendon-jerks were the same on both sides, and there appeared to be no difference in the character of the radial pulse on the affected side.

Conclusion

A series of 25 cases of fracture of the first rib is presented; these fractures had occurred in the majority of cases without symptoms, and showed a preponderance in young adults between the ages of 18 and 19. Cases that present with acute and severe symptoms conform to a characteristic clinical picture.

The radiological picture is constant in its site, the fracture occurring always in the region of the scalene tubercle of the rib. Callus seems to be rather slow in developing on the whole, and cases of non-union are not uncommon.

In no case could damage to the brachial plexus or subclavian artery be demonstrated clinically.

I would like to thank Colonel Handy, Officer Commanding the Cambridge Military Hospital, Aldershot, for permission to submit this article. My thanks are also due to Major McKelvie, radiologist at the above hospital, for his help and co-operation in producing the article, also to Lieutenant-Colonel A. Whyte and Major Hedley Hall for their advice. In addition I am grateful to Mr. Dillwyn Evans, consultant orthopaedic surgeon, Royal Infirmary, Cardiff, and Dr. J. G. H. James, orthopaedic registrar of the same hospital, for their advice and kind permission to include one of their cases in the series, and to Mr. Arthur Welch for the photographs.

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Medical Memoranda

Chronic Porphyria

This report describes a case of chronic porphyria in which photosensitivity of the skin and episodes of abdominal colic and jaundice occurred in adult life without the appearance of neurological or psychotic manifestations. There was no evidence that this case belonged to the familial group of porphyrias; rather did it resemble the chronic porphyrias described by Taylor, Solomon, Weiland, and Figge (1946) and Gray, Rimington, and Thomson (1948). An important feature was the extreme severity of the illness at one stage.

CASE REPORT

A woman aged 38 was admitted to hospital on September 4, 1947, with severe malaise, abdominal pain, jaundice, and a vesicular eruption on the face, arms, hands, and legs. The illness had begun on July 24, 1947, with malaise, nausea, vomiting, and upper abdominal pain. On July 29 there was angioneurotic oedema of the face and an irritation of the skin over the whole body. The former cleared in two days, but the irritation persisted in varying degree. The urine was thought to be dark at this time; it was definitely dark on August 1 and was reported by her own doctor to contain bile. Jaundice was evident on August 2; it increased in intensity for ten days, then decreased considerably as the patient improved. The bullous eruption first appeared under the tongue on July 29, and on the face, neck, forearms, hands, and legs on August 3 and succeeding days. The trunk remained free of skin lesions, but irritation of the skin was present. The patient remained thus in poor health, with slight varying jaundice, abdominal discomfort, and recurring crops of vesicles until September 4, when sudden deterioration in the condition with severe abdominal pain and deepening jaundice caused her admission to hospital.

Vesicles continued to appear in crops on the exposed areas of the skin, each vesicle often preceded by a pricking sensation in the skin at that site. The haematological, serological, and biochemical investigations were negative, except a raised serum bilirubin at 4.4 mg. per 100 ml. The vesicle fluid showed some neutrophils; culture was sterile. No increase in faecal or urinary porphyrins was detected at this time. Exposure to ultra-violet light did not produce new vesicles. Over a period of two months there was a slow improvement, in no way affected by the various therapeutic measures except that of covering the exposed skin areas with cream and gauze; this measure quickly reduced the incidence of vesicles.

Detailed inquiry revealed that the patient had not felt well during the early summer and had not enjoyed being in the sunshine; despite this she spent a whole day in bright sunshine before the onset of her illness on July 24. In previous years she had been quite well and in no way affected by sunlight.

From November, 1947, until August, 1948, she was in fair health, though under weight and sleeping badly. She avoided direct sunlight but still had occasional skin irritation followed by the usual vesicle. On a holiday late in August, 1948, she ventured to sit in the open air for a while when the sky was overcast; that same afternoon the skin irritation became severe over the entire body, but worse in the exposed areas. She felt very ill and experienced abdominal pain and vomiting during that night. Next morning there was swelling of the face and hands, and vesicles appeared later. This second day there occurred some darkening of the urine, icterus of the skin, lightening in colour of the stools, and a rapid deterioration in the general condition. She was readmitted to hospital.

The serum bilirubin was 6 mg. per 100 ml., serum alkaline phosphatase 15 King–Armstrong units, and metalloporphyrins were present in the urine in considerable quantity. The condition became very grave before eventual improvement, the most beneficial measure being continuous intravenous infusions of glucose and normal saline solutions. The metalloporphyrins were present in the urine for 40 days and until considerable improvement had taken place. The serum alkaline phosphatase rose to 29 King–Armstrong units before returning to normal.

Two months from the day of onset the patient was again fairly well, but below weight and easily fatigued. She remained below normal in health and had occasional vesicles on the exposed skin. In February, 1949, purely as an empirical measure, 10 mg. of folic acid was given daily on 14 days in every 28 days, from February to September, 1949. During this period she consistently improved in health, and in spite of an unusually sunny summer and moderate exposure to sunlight for short periods there has been no suggestion of recurrence of symptoms; no metalloporphyrins have been detected in the urine or any excess of these in the faeces.

COMMENT

The sequence of events in cases of chronic porphyria or porphyria cutanea tarda has been discussed by Gray, Rimington, and Thomson (1948). The above case shows how mild irritation of the skin can be present for long periods with occasional skin lesions, and how the onset of hepatitis with jaundice can then increase the gravity of the illness. During this phase the most valuable therapeutic measures were the skin protection throughout with creams and coverings, and the administration of glucose–saline intravenous infusions at the critical stages of liver damage. The more recent improvement in the patient's condition coincident with the administration of folic acid was quite striking, and her survival in health through the summer of 1949 was a great relief to all concerned. There is at present no means

of assessing the actual part played by the folic acid: recovery may have been coincidental, but this problem is worthy of further consideration.

ARTHUR J. THOMAS, M.D., M.R.C.P.

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Reduction *en masse* of a Strangulated Inguinal Hernia

The clinical picture of continuing intestinal obstruction after the reduction of external herniae is well recognized and a correct pre-operative diagnosis can usually be made. The following case is of interest in that five days elapsed from the time of reduction to operation, and yet the bowel remained viable. Such a condition has been reported previously and longer intervals have been recorded. Walsham (1901) records cases in which the interval was of two months' duration, and in Professor Grey Turner's (1903–4) case the interval was several months. In such cases the hernia remained impacted, although no actual strangulation of the contents occurred.

CASE REPORT

A man aged 68 was admitted to the Central Middlesex Hospital on September 21, 1944, about 9.20 p.m. He had suffered from a right inguinal hernia for three years, for which he had worn a truss for 18 months. During the week previous to admission he had a heavy cold with a troublesome cough, and two days before admission the hernia came down and was larger and more painful than before. At the same time he had an attack of central abdominal pain and vomiting. It was nearly two hours before he was able to reduce the rupture himself. This relieved the pain a good deal, but intermittent colicky pains recurred at intervals throughout the next two days. He vomited twice each day. His appetite went and he took only fluids by mouth. The bowels ceased to act for faeces or flatus. Apart from numerous winter coughs there was nothing significant in his previous history.

On examination he was found to be a rather frail old man with a heavy cold and troublesome cough. Signs of subacute bronchitis were present, but a subsequent radiograph showed no other changes in the lung fields. There was a slow auricular fibrillation and the blood pressure was 140/90. There were signs of moderate dehydration. The tongue was dry and furred and the skin of the abdominal wall somewhat inelastic. The abdomen showed moderate central distension with some tenderness in the right iliac fossa. Peristalsis was present and moderately active, and a succussion splash could be detected. Rectal examination showed no abnormality. There was no evidence of an external hernia. The external ring of the right inguinal canal was very lax.

The patient's general condition was poor, and a Ryle's tube was passed intranasally and suction started. Intravenous glucose-saline was begun with a slow drip. The next day his signs were unchanged and a straight radiograph of the abdomen and chest was taken. The erect film of the abdomen showed numerous small-bowel fluid levels, and in the supine position gas shadows were present in the lower ileum but not in the caecum.

An enema was given and some faeces were passed, but no flatus. His general condition began to improve and the intravenous drip and gastric suction were continued.

On September 23 laparotomy was carried out through a right paramedian incision. The caecum was collapsed, and on following the collapsed terminal ileum proximally about 2 ft. (0.6 m.) from the ileocaecal valve this loop was found to enter a peritoneal pouch and the whole mass was delivered into the wound. With retraction it was clear that the condition was reduction *en masse* of a right inguinal hernia into the abdominal cavity. The loop of bowel which was markedly congested was reduced manually by distal squeezing as in reduction of an intussusception; it was found to be viable and was returned to the abdomen. The hernial sac, which had been partially turned inside out and appeared as though on a pedicle, was ligated and transfixed at the internal ring from within the abdomen. The canal was not explored extraperitoneally for repair owing to the age and poor general condition of the patient. The cause of the obstruction was the intact internal ring, which had been displaced backwards with the sac.

The bowels acted with an enema on the second day, and thereafter continued normally. The cough was troublesome, but serious chest complications were avoided. The wound developed a superficial infection and discharged for a few days, but was healed at the end of three weeks.

COMMENT

The condition of reduction *en masse* with strangulation is still uncommon enough to warrant recording to remind surgeons that such a condition can occur and that it may be produced either by the doctor or by the patient. The latter condition has been referred to as auto-reduction *en masse* (Cooley, 1942, and, although considerable force is usually necessary to bring this about, such force is sometimes used in an endeavour to avoid an operation in a patient such as a chronic bronchitic. Pearse (1931) in a review of 190 cases gives the incidence as 1 in 13,000 cases of inguinal herniae. He found that reduction to a properitoneal position was by far the commonest type seen. Nason and Mixter (1935) stressed that in none of their five cases was undue force used in the reduction Such cases are closely allied to reported cases of spontaneous reduction *en masse* (Crowe, 1943), the mechanism of which remains unexplained but can easily be visualized in a hernia which is inadequately controlled by a truss and constantly recurring, often whilst the truss is actually being worn.

The case presented was not of the common properitoneal variety but of the less common intraperitoneal type. The following conditions—(*a*) a mobile sac, (*b*) a lax internal ring, and (*c*) lax parietal peritoneum posterior to the ring—will allow a reduction *en bloc* into the peritoneal cavity of the internal ring and the sac, which is turned inside out "like the finger of a glove." There was no evidence of rupture of the sac at the neck, and presumably enough tension remained at this level to constrict lightly the bowel content, which, although completely obstructed to faeces or flatus, remained viable after such constriction for five days.

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Dr. Trias de Bes, vice-president of the Royal Spanish Sporting Club, is travelling to Manila with the club's soccer team, which has arranged a football match there, to lecture to the Medical Faculty of the Philippines on work done recently in Barcelona on subacute bacterial endocarditis. The work was done in the municipal hospital for infectious diseases, of which the lecturer is director.

Reviews

ANTIBIOTICS

Antibiotics. By H. W. Florey, M.D., F.R.S., E. Chain, Ph.D., F.R.S., N. G. Heatley, M.A., Ph.D., M. A. Jennings, M.A., B.M., A. G. Sanders, M.B., D.Phil., E. P. Abraham, M.A., D.Phil., and M. E. Florey, M.B., B.S. Vols. I and II. (Pp. 1,774; 265 figures. £8 8s.) London: Geoffrey Cumberlege, Oxford University Press. 1949.

Most of the team of workers at Oxford to whom we owe the establishment of penicillin as a chemotherapeutic agent have pursued further studies in antibiotics in the decade which has elapsed since then. Not only have they made large contributions to the expanding study of penicillin itself, but they were among the first to explore the plant kingdom in the now world-wide search for sources of new antimicrobic agents. Among such substances studied at Oxford have been mycophenolic acid, proactinomycin, helvolic acid, the colicines, ayfivin, and alvein: most of these have been submitted to exhaustive examination, and two at least have almost proved to be winners in the chemotherapeutic field. Hence no group of workers in this country and probably none elsewhere is in a better position to write the leading authoritative work on antibiotics, and this further task they have now completed..

The entire treatise is to consist of three volumes: the third, yet to be published, will be entitled *Clinical Applications of Antibiotics.* Volume I begins with a historical introduction, reviewing the study of antibiosis from its origins in folk medicine and the work of such pioneers as Pasteur, through half a century of varied but groping efforts to attack one micro-organism with another. How long this story is few people could have had any idea until Florey reviewed it in the Lister Lecture of 1945, published in the *Journal.* In this chapter it is told in greater detail with interesting embellishments. There follows a section on general experimental methods—the detection, extraction, and assay of antibiotics, the measurement of sensitivity to them, and their use in selective media. The remainder of this volume is a review of the characters of all known antibiotics produced by fungi, actinomycetes, bacteria, and higher plants—quite bewildering in its extent and impressive as an orderly condensation of a vast amount of diverse information. There are some strange names among the lesser antibiotics, among them the acids quaintly named frequentic, hirsutic, kojic, and nudic.

The large second volume is mainly about penicillin (omitting its clinical use), from its production and purification to its action on bacteria and its behaviour in the body. This section contains a much fuller account than any yet published of the long process by which the molecular structure of penicillin was ascertained. Although even more liberally interspersed with complex formulae than the rest of the book, this makes fascinating reading. Streptomycin is then described on the same lines. There are two concluding chapters on general aspects of the subject, an appendix embodying recent new information, a table occupying 29 pages giving the main characters of the principal antibiotics, and nearly 200 pages of bibliography and indices.

The appearance of such a work is a major event in medical literature: indeed it is difficult to think of any in which a topic of such magnitude has been treated so exhaustively. It is an apparently complete review of everything written on its subject up to a date in 1948, and if any criticism can be offered it is only that authors are occasionally quoted whose work is so trivial as scarcely to deserve mention. It suffers from the drawback—inevitable in books on rapidly advancing subjects—that progress has outstripped the efforts of the publisher; chloromycetin is adequately described, but aureomycin has just missed full recognition.

To anyone interested in progress in antibiotics these volumes will be indispensable. The reader will have every confidence in the authors' assessments, and he may depend on the highest standard of accuracy in quotation. The investigator who believes that he has discovered a new antibiotic may easily find by reference to these pages that he has only rediscovered an old one. Any inquirer after an obscure point in connexion with penicillin or streptomycin will find the answer he needs, if it is known. In the United States particularly, where an originally British discovery has been exploited so widely and so profitably, this work will command universal respect and possibly find its largest market.

L. P. GARROD.

MANAGEMENT OF DIABETES

Diabetes and Its Treatment. By Joseph H. Barach, M.D., F.A.C.P. Oxford Medical Publications. (Pp. 326; illustrated. £2 10s.) New York and London: Geoffrey Cumberlege (Oxford Medical Publications). 1949.

The author states in his preface that this book offers the general medical man a clinical approach to an understanding of diabetes and its treatment. The arrangement of the text is unusual in that the complications of diabetes precede the routine treatment. The first chapter consists of a chronological historical survey, an interesting introduction. Aetiological factors are considered in some detail, but the brief mention of the pituitary and adrenal glands in this connexion, the latter being dismissed in less than six lines, is in striking contrast to the consideration given to occupation, residence, geographical distribution, and parental longevity. This lack of balance is noticeable throughout, and is particularly evident in the chapter on complications: the space allotted to vibratory tests in peripheral vascular disease is out of all proportion to the attention paid to such important subjects as retinitis and tuberculosis. Renal glycosuria is placed last among the non-diabetic glycosurias, and in a very inadequate description of this condition no mention is made of renal threshold.

The modern views on the treatment of diabetic coma are given in detail and the reader is left to choose between the methods described. The duties prescribed for the intern or resident in charge of a case of coma are worthy of note—they include estimation of blood sugar, urea nitrogen, blood chloride, cholesterol, blood acetone, quantitative urine sugar, and total leucocyte and differential counts. In the chapter on pregnancy, hormone therapy as practised by Priscilla White is advocated, but there is no reference to the work of Smith and Smith nor to the recent important findings on the pre-diabetic state.

The last 100 pages, which describe a system of diets, add more to the bulk than to the usefulness of the book. A simple description of the principles of dieting with adequate food tables is all that is now generally held to be necessary to achieve good results. This unbalanced but not uninteresting account of diabetes, in spite of its size, cannot be regarded as a work of reference, and on account of it can hardly be recommended for the majority of general physicians.

WILFRID OAKLEY.

A SOUTH AFRICAN TEXTBOOK

Public Health Bacteriology and Parasitology. By C. G. Booker, M.D., D.P.H. (Pp. 254; 108 illustrations. £1 15s., plus 1s. postage.) South Africa: Central News Agency, P.O. Box 1033, Johannesburg. London: Gordon and Gotch, Ltd., 75, Farringdon Street, London, E.C.

The author, who is Deputy Chief Health Officer of the South African State Railways, has collected in one volume descriptions of the bacteria, protozoa, helminths, molluscs, arthropods, and vertebrates which cause disease or are vectors, hosts, or reservoirs of infecting agents in that part of the world. The book is frankly one for the beginner, so that the accounts mention only the outstanding distinguishing characters of the species. These are very briefly described and clearly illustrated by drawings or coloured plates. It is not designed for the whole-time pathologist and must be judged from the standpoint of the workers for whom it was written, the health staff of the railways. There is no doubt that these readers will find it a useful and (with minor exceptions) an accurate book for study and reference.

In the absence of more detailed knowledge of the duties of those for whom the work is intended, one is reluctant to be unduly critical. It seemed, however, that the author had fallen short of producing either a concise laboratory guide or an account of the principles of infection and the control of the parasites he describes. For example, a worker who needs to know the fermentation reactions of the salmonellae (which are given) should also know the modern methods of isolation of these bacteria, which are not mentioned. The methods described for the bacteriological examination of water and of air are unlikely to give reliable results, and the worker may get the impression that he can assess the quality of milk by incubating it with "a small amount of methylene blue" Botanical and zoological classification is unnecessarily stressed, but viruses are dismissed in four pages. It was unfortunate that I should have opened the book at the plate facing page 65, in which the names of the species in both captions are mis-spelt.

The section on protozoology is probably the best. Apart from the possible faults of selection which have been mentioned, the book presents a useful summary of the subject and may meet the needs of the isolated worker in the Tropics. It would not be claimed that it is a suitable book for the public health student in this country in these days, when he is more concerned with epidemiological principles and the control of infection than with the details of laboratory procedures.

J. C. CRUICKSHANK.

A HISTORY OF JOHNS HOPKINS

The Story of Johns Hopkins. By Bertram M. Bernheim, M.D. (Pp. 274. 12s. 6d.) Kingswood, Surrey: The Windmill Press. 1949.

Johns Hopkins is a name to conjure with in medical circles. In his racy American Dr. Bernheim enthusiastically surrounds it with romance, and makes the school a living organism in the eyes of those to whom it had previously been only an honoured name.

I have only one fault to find with the book. Although the author firmly disclaims any pretension to be the historian of the school, and says his purpose is mainly to describe "the great four," in my opinion the value of his story would have been greatly enhanced if he had told us more about the school's beginnings. I am still ignorant of the original intentions of Johns Hopkins, of the man himself, of how much money he left to found the school, and what restrictions, if any, he placed on his trustees. However, Dr. Bernheim does tell us that the unique position of Johns Hopkins was the result of its "starting from scratch with new blood and new ideas"; and he makes it plain that its worth was due to Welch, Osler, Halsted, and Kelly. His account of these men is that of a hero-worshipper. It was their ideas that were embodied in the work of the hospital which drew ambitious young men from all parts of the United States. It was they who trained these men to go out to spread the fame and traditions of their school. Welch, the first-comer, is declared to be "the greatest medical statesman of America": it was Osler, always spoken of as "the chief," who "gave of himself to the students, more of himself than any other member of the faculty," and was its "soul."

Although Dr. Bernheim is convinced that there never was such an inspiring school, he is critical about some of its policies and methods. He complains that in making appointments to "the hierarchy" (yet he leaves us in no doubt that it was a hierarchy) the trustees never consulted the staff, and the top positions were almost always filled by outsiders. It was commonly said that "if men ever wanted to get recognition from their Alma Mater they should accept outside offers," and many who took this advice did return.

Dr. Bernheim has interesting stories to tell about all the leading men of the school that he met during his forty years' connexion with it. He thinks it was never quite the same after Osler left it, a tired and overworked man. He is critical about some of those who followed, and characteristically enthusiastic about others. He was a rebel when the trustees adopted the whole-time system for teachers, and it took him some years to become reconciled to the idea. He now believes that all medical teachers in the future should give their full time to their duties, though still of the opinion that the system tends to make its subjects unduly interested in the scientific, as contrasted with the human and practical, side of practice. Many naturally turn to teaching and research, but they will always be a minority; and those who enter private practice are liable to be handicapped in competition with their colleagues.

I cannot deal adequately in the space with such a full and absorbing book, but can cordially recommend it to anyone who would like to know more about the Johns Hopkins and its famous staff. There are excellent portraits of the Founder, the institution, "the big four," Harvey Cushing, and John Finney.

ALFRED COX.

PSYCHIATRY FOR THE GENERAL PRACTITIONER

Practical Lessons in Psychiatry. By Joseph L. Fetterman, M.D. (Pp. 342. £1 10s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1949.

Psycho-Analysis. By Edward Glover, M.D. Second edition. (Pp. 367. 15s.) London and New York: Staples Press. 1949.

These two books are markedly contrasting in style and content, yet they are to some extent complementary. Both are written for the general practitioner. The American book is superficial, exuberant, and plentifully interspersed with illustrative case histories. The author gives a short survey of mental illness, including neurosyphilis, epilepsy, and the effects of head injury (the latter chapter containing a comprehensive section on treatment). Dr. Glover, on the other hand, in this second edition of his work on psycho-analysis first published ten years ago, has brought the subject matter up to date in a closely reasoned account without case illustrations.

The busy practitioner will certainly find the American book easier and perhaps pleasanter to read. It will give him a guide to the forms of mental illness and the ways in which they may be treated, but he may be content to leave the choice of these methods and their application to the specialist. He may feel much attracted to the apparent ease, practicability, and immediate good results of the new physical methods. The more thoughtful practitioner, however, like the more thoughtful psychiatrist, may feel that there is more in this very complex subject than this. The latter group of psychiatrists admit that the modern short cuts can at best "cure" a few mild cases and relieve a larger number of patients of some symptoms, or make them more accessible to the treatment that offers any hope of complete cure—some form of analytic psychotherapy.

It is generally admitted that, whatever modification the individual therapist may favour, the basis of his work, of which he cannot afford to be ignorant, is the Freudian theory and practice. He must therefore welcome this new edition of Dr. Glover's book. He will not find it easy reading unless he is already fully conversant with the subject, and it is difficult to see how the general practitioner will follow any of the last section, which gives directions for diagnosis, prognosis, and selection of analyst, without this knowledge. If he carefully and conscientiously follows the previous chapters, however, he will go far to acquire this information.

If the reader accepts the analyst's claim to the truth of the primary postulates—the oedipus complex, the castration fear, the oral, anal, and genital stages of infantile mental development, the regression and inhibitions in face of frustrations throughout life, and the advances and outbursts, the retreats, and the suppressions of love and hate which result—he will find that mental illness fits with remarkable logic and neatness into the scheme built on these foundations. He may find the premises difficult to accept if he has no experience of psycho-analysis himself, either subjectively or objectively, yet he may be assured that a very large volume of evidence in support of the theory has now been accumulated by those who take psycho-analysis seriously. The author makes no claim to universal success for the method which he firmly believes is the only comprehensive and potentially successful means of treatment of mental illness, admitting that only the few have the time, the means, and the will to get well to submit to the full discipline. He has little use for short cuts of any sort, and points out that as the deviations responsible for the psychoses have their origin before the age of 3 it may be very difficult to reach and to resolve the complex entanglements which are responsible for these diseases. In both diagnosis and prognosis, therefore, it is more important to estimate how far back in the mental development of the individual the roots of the illness lie than to give them a name such as schizophrenia or obsessional neurosis.

The chapter on child analysis shows how much work is still necessary to complete the structure of psycho-analysis. We may hope that when the next edition of this book appears the gaps in our knowledge will have closed still further.

R G. GORDON.

The catalogue of the exhibition at the Wellcome Historical Medical Museum celebrating the bicentenary of the birth of Edward Jenner has been published by the Oxford University Press (London: pp. 38; 2s.). This catalogue is not only a guide to the exhibits, but contains bibliographical and other details which will be useful for reference purposes.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

The Dawn of Scottish Social Welfare. By T. Ferguson. (Pp. 321. 21s.) London and Edinburgh: Thomas Nelson. 1948.

Biochemical Society Symposia No. 3. Partition Chromatography. Edited by R. T. Williams and R. L. M. Synge. (Pp. 103. 6s.) Cambridge: The University Press. 1949.

The Personality of William Harvey. By G. Keynes, M.D., F.R.C.S. (Pp. 47. 5s.) Cambridge: The University Press. 1949.

In Search of Alice. By G. Bousfield. (Pp. 169. No price.) London: Temple. 1949.

Outlines of Biochemistry. By R. A. Gortner. Edited by R. A. Gortner, jun., and W. A. Gortner. 3rd ed. (Pp. 1,078. 60s. or $7.50.) London: Chapman and Hall. 1949.

Stomach Disease as Diagnosed by Gastroscopy. By E. D. Palmer, M.S., M.D. (Pp. 200. 42s.) London: Henry Kimpton. 1949.

Bennett's Materia Medica and Pharmacy for Medical Students. By R. R. Bennett, B.Sc.Lond., F.R.I.C. Revised by H. G. Rolfe, B.Sc.Lond., F.R.I.C. 5th ed. (Pp. 276. 16s.) London: Lewis. 1950.

The World Next Door. By F. Peters. (Pp. 320. 12s. 6d.) London: Victor Gollancz. 1950.

Handbook of Digestive Diseases. By J. L. Kantor, M.D., F.A.C.P., and A. M. Kasich, M.D., F.A.C.P. 2nd ed. (Pp. 658. 75s.) London: Henry Kimpton 1949.

Diagnosis and Treatment of Brain Tumors and Care of the Neurosurgical Patient. By E. Sachs, A.B., M.D. 2nd ed. (Pp. 552. 105s.) London: Henry Kimpton. 1949.

The Sexual Perversions and Abnormalities. By C. Allen, M.D., M.R.C.P., D.P.M. 2nd ed. (Pp. 346. 25s.) London: Geoffrey Cumberlege. 1949.

The Middlesex Hospital, 1745-1948. By H. St. George Saunders. (Pp. 100. 8s. 6d.) London: Max Parrish. 1949.

Vitaminology. By W. H. Eddy, Ph.D. (Pp. 365. 46s. 6d.) London: Baillière, Tindall and Cox. Baltimore: The Williams and Wilkins Company. 1949

The Natural Bent. By P. B. Barringer. (Pp. 280. $3.50 or 28s.) London: Geoffrey Cumberlege. Chapel Hill, N.C.: The University of North Carolina Press. 1949.

The Chicago-Cook County Health Survey. By the United States Public Health Service. (Pp. 1,317. $15 or 120s.) London: Geoffrey Cumberlege. New York: Columbia University Press. 1949.

Normal Values in Clinical Medicine. By F. W. Sunderman, M.D., Ph.D., and F. Boerner, V.M.D. Pp. 845. 70s.) Philadelphia and London: Saunders. 1949.

Clinical Electroencephalography. By R. Cohn, M.D. (Pp. 639. 119s. or $14.) New York, London, and Toronto: McGraw-Hill Book Company, Inc. 1949.

Mobilization of the Human Body. By H. E. Billig, jun., M.D., F.I.C.S., and E. Loewendahl, M.A., Ph.T. (Pp. 65. 16s.) Stanford, Cal.: Stanford University Press. London: Geoffrey Cumberlege. 1949.

Médecine du Travail. By C. Simonin and others. (Pp. 913. 2,800 francs.) Paris: Librairie Maloine. 1950.

Legislacion Sobre Seguridad e Higiene del Trabajo. Apendice 1948. (Pp. 167. No price.) Madrid: Seccion de Prevencion de Accidentes e Higiene del Trabajo. 1948.

Estudios sobre la Circulación Renal. By J. Trueta, M.D., D.Sc. (Pp. 208. 180 pesetas.) Barcelona: Publicaciones Médicas. 1949.

Der Arzt in der Krise der Zeit. By K. Rom. (Pp. 181. No price.) Vienna: Franz Deuticke. 1949.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY FEBRUARY 4 1950

ADRENOCORTICOTROPHIN THERAPY

The first excitement roused by reports of the dramatic results obtained with cortisone and adrenocorticotrophin (ACTH) is now beginning to fade, and the effects of therapy are being carefully examined. As Professor J. W. McNee[1] recently wrote in this *Journal*, the discovery of the clinical effects of these compounds is something of quite fundamental importance in medicine, and as work continues the range of conditions in which good results may be expected is widening and now includes gout, dermatomyositis, scleroderma, asthma, and probably myasthenia gravis.[2] But experience with these substances has been so brief and the number of cases that could be treated so few that appraisal of their potential dangers and therapeutic inadequacy has not been possible, though enough was known of their metabolic effects to predict some of the possible results of their use. Supplies of ACTH and cortisone in the United States are large enough to justify continued trials to determine the range of side-effects in practice, for until more is known of these and the long-term results of treatment their therapeutic value cannot be assessed. The most suitable therapeutic regime has also to be determined. Elkinton and his colleagues[3] in Philadelphia have now published some of the disquieting observations made at the conference of investigators sponsored by the Armour Company in Chicago last October. These workers have studied two cases of "juvenile rheumatoid arthritis," two of disseminated lupus erythematosus, two of rheumatic fever, and one each of dermatomyositis and status asthmaticus. Six of the eight patients responded well to the initial administration of ACTH; in four of these six treatment was prolonged, and the condition of the patient with dermatomyositis and of one of the patients with lupus erythematosus improved greatly. The other patient with lupus erythematosus and one with acute rheumatoid arthritis ultimately failed to benefit from treatment. During a 30-day period of observation the patient with status asthmaticus was given three courses of ACTH and responded well. The two patients with acute rheumatic fever did not improve when given three-day courses of 60 and 120 mg. respectively of ACTH daily, though there was positive metabolic evidence of adequate stimulation of the adrenal cortex. The authors rightly observe that this period of treatment might not have been long enough.

It is unfortunate that Elkinton and his colleagues do not state the potency of the particular samples of ACTH used, for it is well known that large variations in potency can occur in different batches. The bulk of the material so far used by investigators in studies of this kind has been supplied by the Armour Company, of Chicago, and the method of assay devised by Sayers for determining its potency depends on the release of ascorbic acid from the adrenal of the hypophysectomized rat.[4] Nearly all the clinical data so far reported are linked with this technique, and there is room for investigation into the relative merits of other methods of assay. At the present time one of the most widely used indices of the potency of the ACTH and of the responsiveness of the patient's adrenal cortex—information about the latter being very necessary when using this material—is the decrease in circulating eosinophils. In general this has appeared to give a valid indication of ACTH activity, but as a test it is the less effective because of lack of knowledge about the dose response curve in individuals with intact adrenals, though Thorn and Forsham[5] have recently published some data. In addition it is not yet known how close a relation exists between this particular index of activity and the therapeutic response in disease. In practice so far this has appeared to be fairly close, and it may well be argued that the action of adrenal cortical hormones on eosinophils (and lymphoid tissue) is closely akin to their effects on the tissues in the diseases which respond to them.

The data of Elkinton and his colleagues shed additional light on this and other points. One of the patients with acute rheumatoid arthritis gained the expected initial benefit from ACTH therapy, but with more prolonged treatment there was increasing difficulty in controlling the signs and symptoms in spite of continued eosinopenia, and attempts at therapy had to be abandoned because of the appearance of some signs of Cushing's syndrome. These authors were particularly unfortunate in their experience with ACTH, for apart from this complication, which is now well known, there were others. In general the metabolic changes produced by ACTH conform to a well-recognized pattern, but the effect on potassium excretion is variable, on some occasions the balance being negative and on others positive. The patient with dermatomyositis, while eating poorly, developed serious potassium deficiency. In the same patient, who was also hypertensive, an obscure episode of encephalopathy occurred during a later course of treatment without any concomitant rise in blood pressure. In addition the sodium-retaining properties of ACTH, which have often been observed, must not be forgotten, and there would appear to be special risks in giving the drug to

[1] *British Medical Journal*, 1949, **1**, 113.
[2] Torda, C., and Wolff, H. G., *J. clin. Invest.*, 1949, **28**, 1128.
[3] *J. Amer. med. Ass.*, 1949, **141**, 1273.
[4] *Endocrinology*, 1948 **42**, 379.
[5] *Recent Progress in Hormone Research*, 1949, **4**, 229.
[6] *Lancet*, 1950, **1**, 117.
[7] Markson, D. E., *J. Amer. med. Ass.*, 1949, **141**, 458. *New Engl. J. Med.*, 1949, **241**, 529.

patients with signs of cardiac damage, such as may be found in disseminated lupus erythematosus. More needs to be known about the susceptibility of patients to changes in electrolyte metabolism, and meanwhile the most careful watch must be kept for such changes.

One of the patients with lupus erythematosus became refractory to the drug after gaining great benefit at first, and at this time an antibody to the ACTH was present in her serum. It is not clear whether this was the cause of the refractoriness or whether the antibody was a true antihormone or a response to some other protein present in the ACTH. In this connexion Kinsell's recent finding that peptides obtained by Dr. C. H. Li from ACTH exert the physiological effect of ACTH has been followed by that of Morris and Morris,[6] who isolated from pituitary-gland extract an apparently homogeneous peptide which is 8.5 times as active as the Armour standard adrenocorticotrophin preparation. Elsewhere in this issue there appears a report of a lecture in which Dr. Li discussed the different methods of biological assay and recent studies of the peptides isolated from ACTH. It remains to be seen whether the peptide fraction is fully as active as the original ACTH and whether it will give rise to the same or fewer side-effects. Their experience with the compound has naturally made Elkinton and his colleagues cautious about advocating the use of ACTH and cortisone for therapeutic purposes. However, the findings of other workers have been more fortunate.[7] Thorn and his colleagues[8] point out that by the use of smaller daily doses of ACTH—40 mg. per day is probably adequate—the danger of Cushing's syndrome is lessened. Rest periods may be required between courses of ACTH therapy, but this has the disadvantage that symptoms and signs of the disease recur after each course. According to these authors gradual reduction of dosage towards the end of a course mitigates this difficulty.

DEATHS FROM INFLUENZA

The official figures concerning deaths from influenza in England and Wales embrace not one but several mysteries. Dr. W. J. Martin's paper in this issue draws attention to some of them. First and foremost, and most satisfactory, deaths from influenza are going down, though naturally there are swings, for influenza does not hit us equally every year. Since 1934 the swings have been rather less in amplitude than earlier, and they have been further apart—only three big peaks in the last 15 years as compared with five in the previous 15 are shown in the graph on page 267. Even more striking and intriguing is the downward trend of the level to which the swings descend, the level of the basic "influenza" deaths of the non-epidemic years. Dr. Martin presents his facts succinctly, but he wisely, though tantalizingly, refrains from drawing inferences. He only tentatively suggests that antibiotics may have had something to do with the falling curve. His figures become more interesting when considered alongside knowledge of recent laboratory findings. Experience has shown that influenza virus A can be isolated very readily in high-peak years, rather less readily in years of low peaks, and hardly ever in intervening "trough" years of low mortality. In fact there is no evidence at all that influenza virus is killing anybody in these years of low mortality. It may be that only the deaths shown in the peaks are true influenza deaths and that those indicated by the part of the chart below the peaks are due to something other than influenza. If so, it looks as if this other "something" was abating even more steadily than influenza itself.

What exactly are these influenza deaths, and why do their numbers so closely correspond with laboratory evidence that influenza A is on the warpath? In the opening pages of this issue Professor C. H. Stuart-Harris, Dr. D. Tyrrell, and Miss Zena Franks try to answer these questions. The deaths which are notified are mostly in patients over 60, many of them with chronic heart disease or bronchitis. Cardiac failure seems to have been the most usual immediate cause of death, and of course pneumonia was common. No difference could be found clinically between deaths occurring during an influenza epidemic and those of an inter-epidemic period. This information was obtained through the help of practitioners who had notified deaths from influenza. It was supplemented by studies of 22 fatal illnesses observed in hospital in Sheffield during the 1949 influenza outbreak: like the practitioners' cases, most of these patients were elderly. From eight of them influenza virus A was actually isolated. As has been noted several times in recent years, coagulase-positive staphylococci seemed particularly dangerous as secondary invaders and were recovered from the lungs of many of the cases, both virus-positive and otherwise. Sad to relate, penicillin and sulphonamides were very disappointing, even though some of the lethal staphylococci were penicillin-sensitive. This fact renders it rather less likely that the use of antibiotics may explain the fall in the influenza death rate.

It is tempting to speculate where influenza is going next. Might it perhaps disappear right off the bottom of the chart? Before so concluding, we need to compare our records with those of other countries. Influenza was so extensive in Western Europe a year ago that it seems unlikely that Continental figures for 1949 will be low; they certainly are not low for Holland. On the other hand, Hungary, which had an almost regular epidemic every alternate year before the war, has had very little influenza since about 1940. There is also the question whether a low incidence is altogether desirable. Dr. Martin's first table shows how influenza gradually faded out during the 45 years from 1848 to 1889, only to flare up into the pandemic of the early 'nineties. The table also shows that since 1890 the yearly toll of

influenza has never fallen to anywhere near the low level of the 'eighties. It was suggested earlier that the deaths in non-epidemic years might be due to something other than influenza. But why should this other something have been much more lethal ever since the influenza of 1890 than it ever was before? And why should it after 50 years or more be growing less lethal now? Clearly there is no shortage of mysteries in this field.

THE MEDICAL RESEARCH COUNCIL

After the war the Medical Research Council published a report of its activities during the period 1939–45. It has now followed this with a report[1] (reviewed on another page) of its work during the first three years of peace. While the war was proceeding the council undertook a number of urgent short-term investigations and other services, most of which lost their importance when hostilities ended. Some of them, however, have continued, notably the work of the committee of the council which is advising on special diets; this will be required for at least as long as food rationing remains. Another emergency development outstaying the emergency which brought it into existence is the Public Health Laboratory Service. This was set up at the outbreak of war in view of the possibility that the enemy might use bacteria as a weapon and also of the danger of epidemics resulting from movements of population. It proved, however, to fill so large a gap in sanitary control that the Ministry of Health placed it on a permanent establishment, and the council, though the task is scarcely within its functions, agreed to continue to administer it. In addition to the central laboratory at Colindale there are now 35 constituent laboratories in England and Wales, as well as a number of special reference laboratories, mostly in London, and the central laboratory is assuming the role of the chief bacteriological institute in the country.

In turning over to a peacetime programme the council found a growing number of problems awaiting solution. Through its various committees it has undertaken research into physiological and psychological factors affecting efficiency in industry; it has carried out important clinical trials with streptomycin; it has sponsored a hearing-aid for adoption by the National Health Service; and it has studied and encouraged the medical applications of nuclear physics. These are special activities, but in fact the work which the council supports or assists leaves no side of medicine, preventive or curative, untouched. This may not be apparent on a casual reading of this report, which embodies separate accounts of the work of the council's principal establishment, the National Institute at Hampstead and Mill Hill, and of 40 research units maintained at hospitals and universities, the council providing the research and technical staff, and the institution the accommodation and facilities. Much of this dispersed work, naturally and on the whole not disadvantageously, overlaps. The work on microbiology, for example, is pursued at half a dozen centres as well as by individual workers to whom research grants are made. But the whole work of which the council has oversight is planned according to a balanced programme, ranging from normal structure and function, through clinical and laboratory studies of disease, methods of treatment and related studies, down to occupational health and social medicine. The ordinary expenditure of the council has averaged £600,000 annually during the three years under review—an impressive total in its way, but equal only to about a six-hundredth part of the money spent in one year on the National Health Service. It is worth recalling that the council itself, then named a committee, was provided for in 1913 under the National Health Insurance Act, just as the Public Health Laboratory Service has been made statutory under the National Health Service Act.

Presumably this is the last report to which the retiring secretary, Sir Edward Mellanby, will attach his signature. Sir Edward Mellanby has been secretary since 1934. The world of science is pretty sharply divided into administration and original work, and it is rare for a man to manifest, as he has done, conspicuous ability in both. The qualities which gained him a great reputation at the laboratory bench he has exhibited also at the executive desk. His work and example will long remain a stimulus to British research, even after his hand has ceased to guide it. Two other retirements from the staff which have already taken place are noted in the report, those of Sir Percival Hartley, an outstanding member of the National Institute team, and Dr. Leonard Colebrook, a member of the scientific staff from the beginning. These recurring gaps are hard to fill. The report mentions recruitment difficulties due to competition of other expanding medical and scientific services, and no doubt the work to be done is always ahead of the supply of workers to do it. Nevertheless knowledge is advancing rapidly, particularly in the fields of biochemistry and biophysics, endocrine and metabolic disorders, and chemotherapy and radiotherapy. Research may have been the Cinderella of medicine, but no one would think so to-day on attending a meeting of, say, radiologists discussing radioactive isotopes or immunologists concerned with antibody response. This report lists the names of 2,000 persons, all of them collaborating in some way with the work of the council, either as members of its expert committees or of its internal or external staff, or as grantees or research fellows. During the three years

[1] *Report of the Medical Research Council for the Years* 1945–1948, H.M.S.O., London.

covered by this report they have produced an impressive volume of literature. The classified bibliographies contain references to about 1,400 papers. Some 50 of these have been published in this *Journal*, but the majority of such communications find their way, properly, into the various specialist journals.

This report itself sets a good example to those who publish their work, for it is well and clearly written. Unlike the reports of some other research institutions, it does not assume in its readers a profound and expert knowledge of the various branches of medical research. It is not written exactly for the man in the street, but it is thoroughly understandable and interesting to the man who has some general scientific background. When an unusual term is reached it is defined. The various investigations are not made to appear as something mysterious and remote. Certainly research does not suffer—it may indeed be greatly furthered—by being made intelligible.

RESEARCH AND THE COLONIAL MEDICAL SERVICE

Medical officers undoubtedly sailed on the early trading and exploring voyages to the Tropics in the times of Elizabeth and the early Stuarts. They were an essential part also of the crews of slave ships throughout the seventeenth and eighteenth centuries, but it was only in the latter century that physicians and surgeons were to be found residing in the West Indies and in the forts and factories which were gradually established in Africa, India, and the Far East. Here their main, and in most cases sole, function was to safeguard the health of the European staffs and such slaves as they possessed. It was only at the Congress of Berlin in 1885 that the colonial powers declared themselves bound "to promote the moral and material well-being of the native populations," thus implying that these powers would attempt to improve the health of all peoples resident in the Tropics. An essential factor in translating this declaration into practice was the establishment in Liverpool and London of schools of tropical medicine fifty years ago and in Germany one year later. These schools have provided a steady stream of highly trained medical officers for the Colonial Medical Service.

Owing very largely to the lack of central organization in this country the work of the Colonial Medical Service has been much less appreciated than that of the medical services of the armed Forces. This has often led to much misconception of the part Great Britain has played in improving health conditions in the Tropics. The time in fact is more than ripe for an accurate and full historical account of the work of Colonial Service medical workers. It is true that surveys of the trends of medical research in the colonies were compiled for departmental use in 1928 and 1930,[1] [2] but in recent years nothing was done to indicate the advances in knowledge made by members of the Colonial Medical Service. An attempt to remedy this defect has now been made by the production of a review and a bibliography of some of the scientific studies undertaken by members of the Colonial Medical Service during the period 1930–47.[3] A brief account is first given of papers published on nutrition, malaria, trypanosomiasis, plague, tuberculosis, leprosy, blackwater fever, typhus, rabies, yaws, tropical ulcers, and the host of other diseases which attack those who live within the tropical zone. Attention is also directed to neurological and psychiatric problems, though as yet all too little is known of the psychology, both normal and abnormal, of tropical peoples. The review thus indicates the wide variety of subjects which have been investigated, and an extensive bibliography of 28 pages shows clearly the vast amount of work carried out by the medical officers of a service almost always overworked and invariably understaffed. One word of criticism may be made of the bibliography. Although quite rightly reference is made to papers in which Colonial Service officers have collaborated with workers who were not themselves members of the Service, yet occasionally papers are recorded which were written wholly by members of the Royal Army Medical Corps, such as that on the sickling phenomenon in the blood of West African natives. On the other hand, some papers written in collaboration by military and civilian medical officers—for instance, the first report on the treatment of tropical ulcer and yaws with penicillin—are omitted. Nevertheless this interesting and important report, at present issued only departmentally, certainly deserves to be made available to the general public, who should be more fully informed of what the Colonial Medical Service has done.

[1] Memorandum on Medical Research in the Colonies (1928).
[2] Memorandum on Medical Research in the Colonies, Protectorates, and Mandated Territories (1930).
[3] A note on some of the scientific studies undertaken by members of the Colonial Medical Service during the period 1930–47, with a bibliography, 1949, Colonial Office (Miscellaneous No. 515).

FATAL IRON POISONING

A few weeks ago Dr. J. H. Prain recorded in this *Journal*[1] the case of a child who died after swallowing a number of pills containing iron, manganese, and copper. Other similar cases have been described, and no doubt there is a danger that young children might be attracted by the appearance of the sugar-coated tablets and swallow them. Elsewhere in this issue (p. 312) there is a report of a fatal case of poisoning by a different preparation of iron. This time the deceased was an adult woman who had taken ½ oz. (15 g.) of iron and ammonium citrate: she was pregnant and apparently took the drug to procure abortion. The official maximum dose is 40 gr. (2.6 g.). Prain found distinct evidence of corrosive action caused by the ferrous sulphate, but in the case now reported no mention is made of the condition of the stomach. The death was ascribed to hepatitis due to iron poisoning. The citrate in iron and ammonium citrate serves as a buffer, so that this preparation occupies an intermediate position between ferrous sulphate and ferrous carbonate. The risk of poisoning is less than with the sulphate, but the absorption of iron, and therefore the efficiency, is also less. Any danger that exists depends on susceptibility and dose. Preparations of iron are not scheduled poisons, but the recent fatalities will no doubt put practitioners on their guard, especially in prescribing iron for children.

[1] *British Medical Journal*, 1949, 2, 1019. See also annotation on p. 1043.

CEPHARANTHINE IN TUBERCULOSIS

The number of substances which are capable of influencing the course of tuberculous infections is gradually increasing. To the sulphones have been added streptomycin and *p*-aminosalicylic acid. Although the latter alone is not perhaps of great effectiveness Vennesland and his colleagues[1] found that *in vitro* the addition of *p*-aminosalicylic acid to streptomycin enhanced chemotherapeutic action. This has been confirmed *in vivo* by Rees and Robson,[2] who have shown that the two drugs have a definite additive effect in preventing the development of standard tuberculous infections of the rabbit's eye.[3] The use of these two drugs in combination may prove to be of value in acute tuberculosis in man by reducing the number of tubercle bacilli before resistance to streptomycin develops.

In Japan during the war years the chemotherapy of tuberculosis has been developing on entirely different lines, and the alkaloid cepharanthine has been shown to have a curative action on tuberculous infections in experimental animals and man. A summary of the results obtained has been given by Hasegawa.[4] Cepharanthine ($C_{37}H_{38}O_6N_2$) is a light yellow powder with a melting-point of 103° C. It is found in the roots of *Stephania cepharantha* and in the stems of *S. sasakii*. The former grows as a vine and the latter is said to resemble a wistaria: both are members of the Menispermaceae family. Cepharanthine, which can be taken by mouth or injected intravenously, has been used in a large number of cases of human tuberculosis. The percentage of "cures" obtained in a series of 290 cases of phthisis was 40.6, but if the patients with additional laryngeal or intestinal lesions were excluded the figure was 48.8. The effects on lupus were marked when as much as 1.0 mg. of the drug was given daily. In laryngeal tuberculosis they were less obvious, but with daily doses of from 0.05 to 0.1 mg. pain and hoarseness disappeared: the best response to treatment was obtained in infiltrative lesions of the vocal cords. Some good results were noted in tuberculosis of bones and of the urogenital tract, and in 10 out of 11 lesions of the eye the curative action of cepharanthine was stated to be remarkable.

The drug was also used prophylactically in Japan in factories and schools. The procedure was to give 0.1 mg. every day for a week and to repeat the course after a week's rest. At the Kokura Arsenal in June, 1942, this prophylactic treatment was given to 2,869 employees. Up till February, 1943, four new cases of tuberculosis had appeared (0.14%), but among 37,040 other untreated employees there were 1,299 cases (3.48%). In 1944 no cepharanthine was used prophylactically and there were 1,096 new cases of tuberculosis, whereas in 1945 when the drug was given to all employees there were only 464 new cases. Similar results are claimed in country towns and villages and in schools. In Toyama there were four primary schools of about equal size. The pupils of two were all given cepharanthine, and during the next six months no new cases of tuberculosis were reported; among the pupils in the untreated schools there were 16 new cases. It is claimed that cepharanthine has also a remarkable effect in all types of leprosy when it is given by mouth. Sixteen of 22 cases of macular and 13 of 27 cases of nerve leprosy are said to have been cured. Although no figures are given, cepharanthine is also reported to be of value in whooping-cough. Further work in other countries will of course be required before acceptance of the claim that cepharanthine is an important drug for the control of infections due to acid-fast bacilli.

[1] *Proc. Soc. exp. Biol., N.Y.*, 1948, **68**, 250.
[2] *Nature, Lond.*, 1949, **164**, 351.
[3] Gardiner, P. A., Rees, R. J. W., and Robson, J. M., *Brit. J. Pharmacol.*, 1949, **4**, 209.
[4] *Jap. J. exp. Med.*, 1949, **20**, 69.

AMPHETAMINE AND APPETITE

The use of *d*-amphetamine to diminish appetite in obesity has been slowly increasing. In some patients amphetamine causes nervousness and, occasionally, fainting attacks, and it should be well known that it is a substance which must be taken only under medical supervision. However, in obesity it has the advantage over thyroid extract that it diminishes desire for food, and various investigations have been made to discover how this effect is produced. When the stomach is empty contractions occur which are known as hunger contractions and which can be recorded in dogs or in men without the use of an anaesthetic after the subject has swallowed a small balloon. Beyer and Meek[1] found that these contractions were inhibited in the dog when *dl*-amphetamine was given by mouth. Since this observation was confirmed in man after a dose of no more than 10 mg., it has been commonly believed that the loss of appetite was due to the cessation of these contractions, though why this should be so was not clear. Harris, Ivy, and Searle[2] tested the view that the contractions give rise to afferent impulses which pass to the brain and stimulate hunger, by cutting the extrinsic nerves to the stomach, both sympathetic and vagal. They found that when amphetamine was given the animals ate less, just as they had done when the drug was given before section of the nerves, and they therefore concluded that the depression of appetite was not due to the change in afferent impulses from the stomach to the brain caused by cessation of hunger contractions.

Sangster, Grossman, and Ivy[3] have also carried out an experiment in which they looked for a relation between the cessation of hunger contractions and loss of appetite. Two dogs were given a standard diet daily at the same time, and records of hunger contractions were obtained in tests carried out once a week. An injection of *d*-amphetamine sulphate or of saline was given and the effect on the contractions observed. Food was then offered, the amount eaten being determined by weighing. Very little relation between the hunger contractions and the desire for food was observed. Thus the contractions had returned to normal one hour after the injection of *d*-amphetamine, but the food then eaten was still very small in amount. Experiments were also made on dogs with gastric pouches, the nerves to which had been divided. In these the injection of *d*-amphetamine did not affect the motility, but the desire for food was removed as usual. The authors

[1] *Proc. Soc. exp. Biol., N.Y.*, 1937, **37**, 74.
[2] *J. Amer. med. Ass.* 1947 **134**, 1468.
[3] *Amer. J. Physiol.*, 1948, **153**, 259.

therefore consider that *d*-amphetamine does not depress appetite as a result of any action on the stomach. They conclude that it is more likely to be a direct central action.

"IMPROVEMENT" OF FLOUR

Since Sir Edward Mellanby first reported in this *Journal* the discovery that dogs fed on flour "improved" by nitrogen trichloride (the agene process) developed hysteria,[1] many attempts have been made to discover whether agenized flour is toxic to man. The evidence is inconclusive, but as a result of an inquiry in the U.S.A. by the Food and Drug Administration the use of nitrogen trichloride as an "improver" was not permitted after August 1, 1949. In this country a committee under the chairmanship of Sir Wilson Jameson, with representatives of the Ministries of Food and Health, the Medical Research Council, and the milling industry, has been reviewing the evidence, and though in human experiments no toxic symptoms have ever been observed the committee has decided that the use of agenized flour in this country should be discontinued. According to a statement issued last week by the Ministries of Health and Food some form of "improver" must be used if the public taste in bread is not to be disregarded, and it has been agreed that chlorine dioxide, which causes no toxic symptoms in animals or man, will take the place of nitrogen trichloride. The change cannot be made quickly, because the necessary plant and supplies of the new improver have to be obtained from the U.S.A., but the milling industry has promised its full co-operation. Though the statement issued by the Ministries assures the public that the present method of treating flour, including agenization, has not proved to be injurious in any way to human health, it is disquieting that not until over three years after a possible danger to health was shown to exist have steps been taken to combat it.

MITRAL STENOSIS IN LATER LIFE

It is often asserted that mitral stenosis is seldom discovered after the age of 50, but this belief is based on clinical impressions rather than statistical evidence: indeed, necropsy records have shown that as many as one-third of all cases of mitral stenosis survive to the age of 50.[2,3] The apparent rarity of mitral disease in later life is partly due to a reluctance to diagnose valvular disease in the elderly and partly because the diagnosis is confused by concurrent hypertension. Cookson[4] has recently described 37 cases of mitral stenosis in patients between the ages of 51 and 77. Only eight of these patients had been correctly diagnosed before admission to hospital. Most of them had auricular fibrillation, normal rhythm being present in only three, and the onset of fibrillation usually marked the advent of cardiac symptoms and failure. The characteristic physical sign was a rough diastolic bruit in the region of the apex beat; the bruit was difficult to hear in some cases, and in others was only audible during the longer periods of diastole. Prolonged and careful auscultation was necessary for the recognition of the murmur. Radiologically the findings were on the whole similar to those in younger patients with mitral disease, but gross backward deviation of the oesophagus was less common, and in two patients there was displacement of the oesophagus to the left instead of to the right. The aortic knob was prominent and frequently showed calcification.

The reason for the long survival of some patients with mitral stenosis is not clear. It has been stated that coincidental hypertension is the main factor in prolonging life.[5] Using a diastolic blood pressure of 100 mm. Hg as a criterion for hypertension, Cookson found the two diseases were present together in half of his cases. Two other factors perhaps deserve further consideration: first, the degree of myocardial involvement during the active rheumatic infection and, secondly, the amount of physical stress to which the patient is subjected later. The importance of stress is suggested by the fact that three-quarters of Cookson's cases were females.

1 *British Medical Journal*, 1946, **2**, 885, and 1947, **2**, 288.
2 Cabot, R. C., *Facts on the Heart*, 1926, Philadelphia.
3 Gelfman, R., *Ann. intern. Med.*, 1943, **19**, 253.
4 *Brit. Heart J.*, 1949, **11**, 155.
5 Levine, S. A., *Clinical Heart Disease*, 1945, Philadelphia.

CONFIDENTIAL AWARDS

The consultants in Northern Ireland, among whom distinction awards have now been distributed, have decided not to allow publication of the recipients' names in the medical or lay press. Like their still-expectant colleagues in the rest of Britain they seem to be embarrassed by this novel method of payment. But presumably the list of recipients will enjoy a limited and confidential circulation in accordance with the advice of the Council of the B.M.A. and the Central Consultants and Specialists Committee.[1]

If the recipients of awards or those who have been passed over feel uncomfortable in the public gaze, a feature unworthy of respect has crept into medicine. The apprehension felt by consultants was reflected in the words of the chairman of the Central Committee's executive recently when he said[2] that it was significant of the atmosphere which surrounded the whole arrangement that secrecy had to be observed. Some such considerations as these must have guided the Council and the Central Committee when they decided that publication in the press is undesirable. These bodies were rightly expressing the wishes of their constituents; but, whatever the necessities of the occasion, the decision is unlikely to be received with equanimity by the profession as a whole or even by the consultants.

There is another point. As this is public money used to provide pensionable increments to income, has not the public a right to know the names of the recipients? We know of no other public award of money that is kept secret—except the presumed payments to members of the Secret Service.

Sir Weldon Dalrymple-Champneys will deliver the Milroy Lectures on "Undulant Fever, a Neglected Problem," before the Royal College of Physicians of London (Pall Mall East, S.W.) on Tuesday and Thursday, February 14 and 16, at 5 p.m.

1 *British Medical Journal, Supplement*, 1949, **2**, 260.
2 Ibid., 1949, **2**, 212.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE INFLUENZAL DISEASES

BY

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The term "influenza," a name given to a group of diseases, conveys one meaning to the epidemiologist and research worker, and an entirely different meaning to the practising physician. We must immediately exclude from a discussion of the complaint the careless application of the term to any feverish condition for which a cause has not been found.

What is the significance of the term to the epidemiologist? He describes an infection by influenza virus A or by influenza virus B. The first is the more virulent organism, is found to cause epidemics at two-yearly intervals, and can be transmitted fairly readily to the ferret from nasopharyngeal garglings. There are probably nine different strains at least which, with the different resistances of the persons attacked, account for the varying severity of the disease in human beings. Influenza virus B tends to be endemic, to cause epidemics at intervals of four to five years, and to produce a milder disease. Transmission to the ferret is very much more difficult, and in fact it was with great difficulty that the virus was originally isolated at all, even though it was at that time (1940) producing a widespread epidemic in North and South Carolina, with several hundred thousand victims.

The detection of virus A and virus B has now been rendered easier by finding a rise in the serum titres of the antibodies through the stage of active infection to convalescence. The problem is complicated by the fact that during an epidemic, side by side with serologically proved cases of influenza, other cases occur which are clinically identical but in which no virus or rise in antibody titre can be found—these may comprise up to 70% of those affected. To overcome this difficulty, these cases have been postulated by the investigator as being due to an infection other than true influenza or to infection with an unidentified influenza Y virus.

So far all attempts at isolating a pathogenic agent from the virus-negative cases have failed. The difficulty of the subject can be appreciated when we realize that virus research as a whole is still in its infancy. Even with influenza virus B there is great variability in its virulence and in the ease of its transfer to experimental animals—and influenza viruses C, D, E, etc., may still remain to be discovered. The enormous strides made in experimental work in the last few years allow us to hope that other specific agents will be identified before long.

The clinician regards influenza in a different light. To him it is a disease occurring in local or widespread epidemics, characterized by the fairly sudden onset of high fever, frontal headache, and pains in the limbs and back, and subsiding (in uncomplicated cases) in two or at the most three days. These epidemics are usually associated with respiratory symptoms, particularly in the winter months, giving the clinical picture of the common type of respiratory influenza. But experienced practitioners describe other forms, such as the gastro-intestinal type, and occasionally an epidemic occurs in which bladder symptoms are prominent. These clinical types are best discussed separately.

Respiratory Influenza

There is no disagreement between the clinician and the epidemiologist on the clinical picture of a typical case, and there has been reinfection of laboratory workers with an influenzal virus from ferrets which has given an attack identical with that in the general population. Such an attack in an adult (more commonly than in children) starts in the course of a few hours with a severe persistent frontal headache, which is soon followed by pain at the back of the eyes. The temperature rises, with a feeling of shivering (less often with a rigor), to 100°–102° or 104° F. (37.8°–38.9° or 40° C.) and the patient feels ill and is glad to go to bed. Within the next few hours pains start in the neck, limbs, and back. There is drowsiness and anorexia, followed by a rawness of the throat and often a dry useless cough. The temperature tends to be higher in the evening than the morning, with a daily swing of 1–2° F. (0.6–1.1° C.); the pulse rate may be raised in proportion to the temperature. During this time the patient looks heavy-eyed, the face is often flushed, the tongue furred, and inspection of the throat shows an injected pharynx (rather than involvement of the fauces or palate). On the second or, more usually, the third day the temperature generally falls and is normal within another 48 hours or so; but some cough may persist for several days, or even a week or more. In an epidemic there are varying degrees of severity of the attack, with corresponding clinical pictures.

Types of Respiratory Influenza

1. *Subclinical Infections.*—These undoubtedly occur, especially in those in intimate contact with sufferers. Such persons are not ill in any way, but proof of infection is given by the subsequent rise in the titre of the antibodies in their blood. Clearly, they are likely to be at least temporary carriers of infection.

2. *With Prominent Bronchial Symptoms.*—The typical attack as described above is associated with pharyngitis and tracheitis in most cases. In a proportion, which varies in different epidemics, retrosternal soreness and pain become more pronounced, the cough continues, a small amount of mucoid or mucopurulent sputum appears, the lungs show a number of rhonchi with coarse and even fine rales, and the fever does not begin to settle on the third day—indeed, on the fourth or fifth days the temperature may rise and remain high for a total of a week or more. During this phase there is a tracheo-bronchitis, and often a bronchiolitis, unassociated with clinical or radiological evidence of pneumonia. Streaks of blood may appear in the sputum, which is quite different from the rusty sputum of pneumonia. In these cases sweating may be profuse towards the end of the day. It is my impression that some patients, particularly those past middle age, always tend to show these lung signs in any subsequent attack of influenza.

3. *With Pneumonic Symptoms.*—Pneumonic symptoms and signs may follow on the third day or fourth day, or even a day or so later, when the temperature has already shown definite signs of settling. This change is associated with a sharp rise in temperature and a rapid deterioration in the condition of the patient. Simultaneously, pain in the chest, and an increase of cough, respiratory distress, and cyanosis coincide with signs of patchy consolidation, particularly at

the lung bases. The frequent occurrence of haemorrhagic peribronchiolar areas of pneumonic consolidation, particularly those located under the pleura, accounts for the chest pain and the considerable amount of blood which may be found in the sputum. Even where definite signs of consolidation are absent, the clinical suspicion of this complication is almost always confirmed by radiography. In a number of these cases, and in some epidemics, the severity of the toxaemia may cause acute pulmonary oedema with severe cyanosis, or circulatory failure with a rapid thin pulse and a low blood pressure. These pneumonic complications are sometimes due to the influenza virus alone, but more usually they are the result of secondary infections with pneumococci, *Staphylococcus aureus*, haemolytic or non-haemolytic streptococci, or *Haemophilus influenzae*. The organism is often the same in a particular epidemic, but varies from one epidemic to another.

Other Complications

Other complications are encountered after this respiratory type of influenza. In health, and even in those suffering from the common cold, there is a substance in the nasal secretions which inactivates the influenza viruses. Once the viruses have overcome this, they exert a profound destructive effect on the epithelium of part or whole of the entire respiratory tract. This helps to explain the nasal sinusitis, the slow convalescence, and the undue susceptibility to the common cold or other respiratory infections that frequently follow influenza.

A bronchitic type of asthma and the symptoms of bronchiectasis are dated from an initial influenzal attack by some patients. A true influenzal myocarditis may occur, and the virus of influenza has been isolated from the heart muscle of those dying from this complication. This explains the cardiac dilatation, poor heart sounds, premature beats, and occasional temporary true heart-block that may be found. More difficult of explanation is the cardiovascular asthenia which is such a common complaint. When the patient begins to get about, and particularly when he starts work, he complains of feeling unduly tired, of an ache in the muscles of the legs on effort, of palpitation, and even of precordial distress—symptoms which may, especially in women, lay the foundation of a neurasthenic state and even of "cardiac invalidism."

The chief mental symptom is depression, which may be of suicidal intensity. Encephalitis lethargica and the onset of disseminated sclerosis seem to follow in the wake of influenza. On the other hand, influenzal meningitis due to *H. influenzae* is probably quite unconnected with the influenzal viruses.

Treatment

This resolves itself into dealing with the symptoms and the complications. There is no specific therapy, but now that there are antibiotics (such as "aureomycin") which influence some virus infections there is the likelihood that one will be discovered which will be of benefit in infections with the influenza virus.

Symptomatic treatment consists in putting the patient to bed and insisting that he remains there until his temperature has been normal for at least 48 hours. A freely ventilated room and not too many bedclothes help to keep the skin cool, and when the temperature is high or perspiration is pronounced a blanket bath is very comforting. Care must be taken that the neck is protected; an open jacket or a low-cut nightdress with cold air playing around the neck often makes the tracheitic cough much more distressing and painful. Indeed, the old-fashioned remedy of warm camphorated oil covered by warm wool, applied to the neck twice a day, is a great comfort.

When headache is not severe and the temperature is high, a mixture of sodium salicylate, 15 gr. (1 g.), and dilute solution of ammonium acetate, 4 dr. (14 ml.), helps as an analgesic and antipyretic. The addition of quinine—unless the patient is known to possess an idiosyncrasy to quinine salts—in the form of the ammoniated tincture, 1 dr. (3.5 ml.), is still popular with many practitioners. When the headache is more severe, tab. codein. co. (2) are often successful in giving relief. To combat the constipating effect of the codeine a tablet of magnesium hydroxide should be taken at the same time.

Sleep is important, and many middle-aged or elderly patients find themselves restless and sleepless during the febrile period. For this a combination of tab. codein. co. (1) and Dover's powder, 10 gr. (0.65 g.), is usually effective, unless the patient then perspires too much. In that case tab. codein. co. (1) may be combined with sodium barbitone, 5 gr. (0.32 g.).

The sulphonamides, penicillin, and streptomycin have no beneficial effects on influenza itself, but when secondary invading organisms show themselves full doses of sulphadimidine (2 g. followed by 1.5 g. four-hourly) should be prescribed. Better still is a combination of sulphadimidine (2 g. followed by 1 g. four-hourly) and penicillin, 500,000 units twelve-hourly. If pneumonia supervenes, this dose of penicillin should be given six-hourly. Although the dosage may be reduced after 48 hours, it is always a mistake to stop chemotherapy entirely for at least two or, preferably, three days after the temperature has settled to normal, for fear that the infecting organisms may again become active.

In elderly patients, and especially if the myocardium is not good and the patient is known to become bronchitic readily, a combination of sulphadimidine and penicillin should be given as prophylaxis before bronchitis shows itself. In these cases digitalis folium 1 gr. (65 mg.) twice a day, or Nativelle's "digitaline," 1/600 gr. (0.1 mg.) twice a day, seems to help the musculature of the heart. If by any chance pulmonary oedema develops, venesection and the use of an oxygen tent will be essential in addition to vigorous chemotherapy.

The diet should at first consist solely of fluid drinks, which may be varied as often as possible in accordance with the desires of the patient. At least 4–5 pints (2.2–2.8 litres) of fluid should be taken in the 24 hours. Glucose may be acceptable, but may be slightly nauseating to some.

Before allowing the patient to get up, the practitioner must be sure that the temperature has satisfactorily settled; and in obese and elderly patients an assessment must be made of the condition of the heart muscle. In the convalescent period preparations containing strychnine and the vitamin B complex seem to be beneficial.

Prophylaxis

Prophylaxis with an anti-influenzal vaccine has become a possibility since the viruses have been grown in the amniotic fluid of developing chick embryos. The results of this form of treatment have been variable, and in some epidemics prophylactic vaccination has had little effect. This is due in a large measure to the relative absence of group antibodies and the narrow limits of action of the protecting antibodies produced by different strains of the same virus. Unless many different strains are used in the

preparation of the vaccine the immunity produced is confined within very narrow limits.

After a single dose of vaccine immune bodies appear in the blood, to the more virulent virus A within one week and a little later to virus B. The immunity is relative, and lasts for not more than two months, so it seems most logical to give a single dose of vaccine immediately an epidemic shows itself. As there is no "negative phase" after giving the vaccine, this is a safe procedure. The vaccine contains a certain amount of egg protein, and a preliminary dose of 0.02 ml. should be given to detect susceptible patients. This precaution prevents allergic reactions, which may be severe.

Other Types of Influenza

Influenzal Type of Gastro-enteritis.—It must be emphasized that there is so far no bacteriological proof that this condition is a separate disease entity. It is a relatively easy matter to label certain other epidemics—of Sonne dysentery, for example—as influenzal outbreaks. Yet experienced practitioners are well aware of localized epidemics which do not fit in, clinically or bacteriologically, with attacks of any recognized bacterial type. Like the respiratory type of influenza these begin rather suddenly, with a temperature of 100–102° F. (37.8–38.9° C.), frontal headache, pain behind the eyes, undue perspiration, aching in the back and limbs, a feeling of considerable illness, and prostration. Anorexia, nausea, vomiting with or without abdominal pain, and diarrhoea are special features of this type. Some upper- or mid-abdominal tenderness may be found, but blood and mucus do not appear in the stools. The temperature does not usually last more than two to three days—a helpful distinction from the enteric fevers—and complications do not occur.

Treatment is on the same general lines as already described: kaolin in doses of 1 dr. (4 g.) four-hourly is of considerable help in controlling vomiting or diarrhoea.

Renal Type.—Other localized epidemics, often labelled as influenzal, conform in their general features to those already described. These symptoms may be associated with frequency and a severe burning pain on micturition. The urine contains pus cells for two to three days, but no bacteria. The temperature drops in two to three days, and recovery is soon established.

RESEARCH IN TRANSITION

MEDICAL RESEARCH COUNCIL'S POST-WAR PROGRAMME

The report of the Medical Research Council just issued[1] covers three post-war years—from October, 1945, to September, 1948. It takes the place of what would normally have been the 32nd to the 34th annual reports of the council. The period covered has been one of transition from urgent wartime preoccupation to more extended investigations and the development of permanent services. Like every other institution, the council has been frustrated in its reconstruction programme by building difficulties which have interfered particularly with the expansion of the National Institute, by the difficulty of obtaining equipment, and by shortage of workers.

The two outstanding features of the council's work since the end of the war have been the development of research into occupational health and the initiation of research projects into the medical and biological aspects of nuclear physics. The report includes an account of many researches into the physiological and psychological factors affecting a man's efficiency at his job—the kind of work which has formed an important branch of the council's investigations ever since the Industrial Health Research Board became part of its organization in 1921. To advise it on the promotion of investigations in this field the council has appointed standing committees in occupational medicine, occupational physiology, occupational psychology, industrial pulmonary diseases, and toxicology. A number of new research units have been set up, notably the Pneumoconiosis Research Unit at Cardiff, now one of the largest of the council's establishments.

Research in Nuclear Physics

In nuclear physics the council has been faced with the problem of organizing research in a largely unexplored field of medical science, the divisions of which may be roughly classified as the protection of the body against the toxic and lethal effects of radioactivity, the use of tracer elements to elucidate biological function, and the study of the radiations associated with atomic and nuclear disintegration as potential curative agents in cancer and other diseases. The question of protection has been remitted to the Radiobiological Research Unit recently set up at Harwell. Work on tracer research with radioactive and stable isotopes is now being carried out at several centres. Up to the end of the period covered by this report most of the isotopes used for medical research were obtained from the United States, but now they have become available in sufficient quantity from the research establishment at Harwell.

As part of its programme of research into the biological effects of ionizing radiations the council has had under consideration the provision of a cyclotron for purely medical use at Hammersmith Hospital. Other machines capable of generating very penetrating rays have been developed, and it is expected that *x* rays generated at somewhere between 10 and 50 million volts will give the radiotherapist the greatest scope for the treatment of cancer. These new machines will make it possible for the first time to carry out clinical investigations with such high-voltage irradiation. Certain investigations of this kind have been planned by a clinical subcommittee under the chairmanship of Lord Horder. It is mentioned that great difficulty is encountered in getting these complicated and costly machines and erecting the buildings to house them.

Special Investigations

The sophistication of food has attracted increasing attention in recent years, and especially the subjection of flour to what is known as the "agene" process. In this treatment flour is mixed with the gas nitrogen trichloride, with the result that the flour is bleached and its protein so altered that much larger loaves of whiter colour and lighter texture can be made from the same weight of flour. About 90% of the flour consumed by the population of this country has been so treated. It has been shown, however, that canine hysteria has occurred in dogs following the consumption of bread or biscuits made of flour treated by the "agene" process, and, although up to the present no ill effects in man have been traced, these are considered a possibility, and it is thought there is a good *prima facie* case for abandoning this method of "improving" flour. At the time the report was written the question was being examined by a committee set up by the Ministry of Health on which the Medical Research Council had representatives. An annotation in this issue (p. 295) comments on a statement by the Ministries of Health and Food on the report of this committee. The statement is to the effect that the use of nitrogen trichloride as a flour improver is to be discontinued; it will be replaced by chlorine dioxide.

At the request of the Ministry of Health the council set up two expert committees to undertake careful clinical tests of streptomycin in tuberculous and non-tuberculous conditions respectively. Full accounts of these trials have been published in the *British Medical Journal*.[2] The present report adds that the work on streptomycin has stimulated a search throughout the world for new natural or synthetic remedies which are

[1] *Report of the Medical Research Council for the Years 1945–1948.* London: H.M. Stationery Office. 1949. 5s. net.

[2] *British Medical Journal*, September 18 and October 30, 1948.

free from its disadvantages. One synthetic compound—*para*-aminosalicylic acid—first tested in Sweden is at present undergoing controlled clinical trials at certain centres in Great Britain.

A reference is made elsewhere in the report to studies at Hampstead on licheniformin, an antibiotic substance found in the subtilis-like organism *B. licheniformis*. This purified licheniformin shows some resemblance to streptomycin in chemical and pharmacological properties. It has a definite effect in suppressing tuberculous lesions in mice, although its therapeutic index (ratio of curative activity to toxicity) is not as favourable as that of streptomycin. It is considered unlikely that it will find therapeutic application in human tuberculosis, except possibly in streptomycin-resistant cases.

Another investigation on which the council was engaged through a special committee was the elaboration of a hearing-aid. After two years of study and experiment the committee recommended a new type of hearing-aid of high efficiency and light weight, capable of being produced cheaply and in large quantities, and likely to help about 90% of the deaf population. This is the "Medresco" hearing-aid which has been available free to deaf persons under the National Health Service Act. "The council has been gratified to learn that to the great majority of patients for whom it has been prescribed it has proved a very satisfactory instrument."

Work of the Research Institutes

The body of this report is occupied with accounts of the work that is proceeding at the National Institute and at the research establishments where the council provides the staff. The National Institute now includes the Harvard Hospital at Salisbury, where the long-term research on the common cold has been proceeding with the help of relays of volunteers. A search, so far unsuccessful, has been made for a susceptible laboratory animal which might play the same essential part as the ferret played in the work on distemper and influenza. The transmission of infection to animals of fourteen species has been tried. Not only have no colds been produced, but the virus has failed to survive for even a few days in the respiratory tracts of several of the species studied.

Other work at the National Institute has included trials of influenza vaccine, studies of vibrios occurring in the natural waters of England and Wales, a study of fatigue and neuromuscular block in mammalian muscle, a chemotherapeutic study of filariasis, and a study of *Leishmania* infections in hamsters and cotton-rats in an attempt to find new drugs useful for the treatment of kala-azar. During the period reviewed two new biological standards have been provided and made available—namely, those for streptomycin and *d*-tubocurarine chloride—and at the end of the period preliminary work on the establishment of three others—oxophenarsine, ABO blood groups, and globin insulin—was practically complete.

The special research units, located at various hospitals and other institutions, have increased from 23 to 40 since 1945. One of the new units for research on pneumoconiosis is at Cardiff. It has been found possible to distinguish two main types of abnormality in *x*-ray films—one a simple pneumoconiosis with generalized fine mottling, and the other a progressive massive fibrosis (PMF), which may be due to some factor other than dust, possibly tuberculous infection.

The Industrial Medicine Research Unit at Birmingham Accident Hospital has concentrated on two of the principal causes of lost time in industry—namely, minor injuries, mostly affecting the hands, and skin diseases. The Chemotherapeutic Research Unit which has been set up at Glasgow chose as its first subject for research the treatment of rheumatic fever with sodium salicylate in an endeavour to settle if possible the question whether the drug cures the disease or, as most clinicians believe, merely relieves the symptoms. The new Electro-medical Research Unit at Stoke Mandeville has devoted itself to a clinical investigation into the cause of bedsores in different patients. The Social Medicine Research Unit at the Central Middlesex Hospital began its work with a consideration of the biological factors influencing infant mortality, the social and psychological aspects of reproductive efficiency, and the occupational incidence of heart disease in middle life. The Research Unit on Climate and Working Efficiency at Oxford has been studying the physiological effects of abnormally hot environmental temperatures. These are but a few examples, taken almost at random, of the work which is proceeding at different centres.

The Public Health Laboratory Service, which has passed from an emergency to a peacetime basis under the direction of the council, has a five-year training scheme for its workers. It is too early yet to estimate the success of the scheme, but it has the merit of a broad outlook and of enabling the young scientific worker to decide which of the many branches of bacteriology he will take up. It is recognized that losses from the Service will inevitably occur, but only good will result if the Service forms a jumping-off ground for appointments in universities and research institutes.

Group research investigations under the auspices of the Service have included such subjects as vaccination against whooping-cough, penicillin and sulphathiazole in the treatment of typhoid fever and typhoid carriers, penicillin in the treatment of diphtheria and its carriers, and the testing of new diphtheria prophylactics.

Medical Research in the Colonies

When the Committee of the Privy Council for Medical Research (which directs the Medical Research Council) was formed in 1920 the Government had clearly in mind that there should be no territorial limitation to the work of the council, and the Secretary of State for the Colonies was made a member of the committee. Since the end of the war a Colonial Medical Research Service has been established, but even when this is in full activity it is felt that the council will still have a large part to play in promoting and developing such studies. A close interweaving of the structure of the new service with that of the council's research organization will be highly desirable. Many members of the council's scientific staff have specialized knowledge and experience which could prove very useful in Colonial medical research. In certain cases there would be an advantage in making the council's research units the home base for investigators whose main work is in the Tropics. This report contains an example of Colonial research conducted in close association with a unit at home—a nutrition field research study in Gambia. Nutritional surveys have also been made in the West Indies. In Basutoland workers for the council have carried out investigations of pellagra which promise to throw light on the relation of the milling of maize to the incidence of the disease.

The report speaks of research opportunities in the Colonial field as of high importance and rich promise. "It is a field which merits cultivation by medical research workers to a still greater extent in the future."

ADRENOCORTICOTROPHIC HORMONE (ACTH)

LECTURE BY DR. C. H. LI

Under the auspices of the Society for Endocrinology a lecture on "The Nature of the Adrenocorticotrophic Hormone (ACTH)" was delivered on January 26 by Dr. C. H. Li, of the Institute of Biochemistry, University of California. The chair was taken by Dr. A. S. Parkes, F.R.S.

Dr. Li reminded his audience that in 1914 Simmonds described cases in which he attributed certain clinical manifestations to pituitary insufficiency; it was now known that the adrenal glands in patients suffering from Simmonds's disease were reduced to half their normal size. In 1932 Harvey Cushing reported cases one feature of which was hypertrophy of the adrenal cortex. Later it was suggested that all the forms of Cushing's syndrome were due to excess of secretion from the hypophysis. Conclusive evidence of the existence of the adrenocorticotrophic hormone came from experiments by Philip Smith, who first demonstrated in rats that adrenocortical atrophy could be corrected by the use of pituitary gland extracts.

The isolation of this hormone in man was made in 1942, and as the hormone exerted its stimulus only on the adrenal cortex it was named the adrenocorticotrophic hormone (ACTH).

All these hormones were protein in nature. This one was highly soluble in water and had a molecular weight of 20,000.

Biological Assay

Three methods were employed for the biological assay of ACTH. The first was called the "repair test." The normal adrenal cortex had three zones, and the effect of ACTH on hypophysectomized rats was to bring about in all these zones a process of repair, changing them back to the normal state. The second method of assay was known as the maintenance test. It depended on the observation of the body-weight and of the adrenal weight in hypophysectomized rats. The hormone was shown to be able to maintain the adrenal weight. In these experiments the injections began on the day of the operation and were continued daily for fifteen days. The adrenal weight was shown to be maintained at the point at which it had stood at operation. If a larger daily dose were given, up to 1 mg., the weight was found to be greater than the normal weight in the untreated rat.

The third method of biological assay was the ascorbic-acid depletion test, and was based on the observation that a single dose of ACTH caused an immediate fall in the adrenal ascorbic-acid content in hypophysectomized rats. Within an hour of the injection of ACTH on the day after the operation there was an immediate fall in ascorbic acid; after three hours it was still very low, but gradually increased. The cholesterol content was also diminished after a single injection, but a rise began after about six hours.

It was important to bear in mind that frequent injections of ACTH were required if the maximum effect was to be produced. This was shown by the simple experiment of injecting a maintenance dose and then reducing the dose level, but giving the injection twice daily instead of once. The results proved that the hormone was utilized very quickly in the animal's body. He had taken a male rat weighing about 200 g., and injected intravenously 5 mg. of ACTH, following this with repeated determinations of the ACTH activity of the plasma. The half-life of the hormone judged by the fall in ACTH activity of the plasma was five minutes. A similar experiment with the pituitary growth hormone suggested that its half-life was about seven hours, so that there was a great difference between the rate at which ACTH was used in the body as compared with others.

The shortness of its life was perhaps due to substances in the body which were capable of destroying the hormone. Some studies had been made *in vitro* in which the destructive effect in plasma, liver, and kidneys had been measured. On incubation of ACTH with these materials the activity practically disappeared. It was satisfying to find that the changes seen in animals were entirely confirmed so far as the work had gone in the human subject. ACTH stimulated the adrenal cortex to produce all the steroids—the deoxy-like compounds, the 11-oxysteroids, and the androgens and oestrogens.

Biological Functions of ACTH

Dr. Li listed the biological functions of ACTH so far observed in animals: (1) Retardation of body growth. (2) Increase of nitrogen and potassium excretion. (3) Increase of free amino-acid content in plasma. (4) Production of glycosuria and hyperglycaemia in rats (though not in cats). (5) Increase of body fat. (6) Promotion of liver hypertrophy, with increase of liver fat. (7) Increase of ketone bodies in urine and blood. (8) Diminution of plasma alkaline phosphatase. (9) Retardation of chondrogenesis and osteogenesis in epiphysis (seen in fibula of cat). (10) Thinning of epidermis and atrophy of sebaceous glands. (11) Involution of thymus and lymph nodes, with depletion of lymphocytes. (12) Decrease of circulating eosinophils. (13) Enhancement of work performance. (14) Beneficial effect on resistance to cold, starvation, and low atmospheric pressure. (15) Enhancement of adrenal regeneration in normal and hypophysectomized rats. (16) Inhibition of insulin effect on glycogenesis in isolated diaphragm of normal rats. (17) Inhibition of development of male accessory organs of the normal rat but not of the hypophysectomized animal.

Chemical Nature of ACTH

One of the remarkable properties of this protein hormone was its resistance to heat. When boiled in neutral or N/10 acid solution there was no loss of activity. Boiling for from two to four hours produced no coagulation, although other proteins not containing carbohydrate coagulated very quickly. With ACTH there was no loss of activity in solution *in vitro* or on assay. This property indicated the great degree of resistance of the molecule.

On boiling it down with strong acid and pepsin and then extracting with ether, a yellow powder was yielded, and it had been shown that the resulting small part of the protein molecule still remained active. The molecular weight of the original protein hormone, as already stated, was 20,000; in this mixture the peptides had an average molecular weight of about 1,200. with an average amino-acid content of 8.

A good deal of work had been done on the separation of this peptide mixture, which could be fractionated easily by paper chromatography. The work, however, was still hardly ripe for discussion. The individual peptides behaved as well as—possibly better than—the original hormone, judging by the ascorbic-acid test.

Clinical Considerations

From a clinical point of view it was important to find out whether this peptide, which had a molecular weight of only 1,200, with an amino-acid content of 8, was active in human subjects. Recently some work had been carried out in Stockholm in which the effect of the peptide in rheumatic cases had been studied, and it was found that in every case the ACTH peptide behaved exactly like the ACTH protein. Indeed, there was some suggestion that the beneficial activity of the peptide was better than that of the original hormone.

The lecturer proceeded finally to give a general summary, which he said was quite incomplete, of the disease and metabolic disorders known up to the present time to be benefited by ACTH. This question had been widely discussed, and only two months ago in New York it was demonstrated that rheumatic fever appeared to be permanently cured by ACTH—that is to say, there was no recurrence. ACTH had been shown to have a beneficial action in rheumatoid diseases of all types, nephrosis, glomerulonephritis, ulcerative colitis, periarteritis nodosa, and asthma and other allergic disorders. Other conditions relieved were aortic regurgitation, tachycardia, and virus pneumonia. There was no doubt that this protein molecule, with its molecular weight of 20,000, could be broken down into a molecule with a weight of 1,200, which was active not only in animals but in the human patient also.

Dr. H. J. S. Folley, in proposing a vote of thanks, thanked also the Ciba Foundation for making the lecturer's journey from Stockholm possible. He said that Dr. Li had made a most important and far-reaching discovery when he found it possible to break down this complicated protein hormone into small fragments, one of which seemed to contain most of the biological activity of the original. There had been repeated attempts to break down the insulin molecule and obtain a peptide, but these had failed. He trusted that the fragment which Dr. Li had worked out would yield to the efforts of the synthetic chemist. The discovery was not only of fundamental importance but of immediate practical concern, and he looked forward to the widespread use of this peptide in the near future, particularly in the treatment of rheumatoid arthritis.

GENERAL ELECTION

The following name should now be added to the list of medical candidates printed in the *Journal* of January 21 (p. 178):

WILLIAM STANLEY RUSSELL THOMAS, Middlesbrough East, Liberal (1919).

General practitioner and barrister-at-law, Lincoln's Inn. M.P. for Southampton from 1940 to 1945. Deputy Chairman, London Liberal National Party, 1937–45. Member, Select Committee on Public Petitions, 1942–4. Member, Select Committee on National Expenditure, 1944.

INTERNATIONAL CERTIFICATES OF VACCINATION AND INOCULATION

AIR TRAVEL HEALTH CONTROL

The Ministry of Health receives complaints from time to time that travellers from the United Kingdom find themselves in difficulty on arrival in other countries because they are not carrying the necessary certificates of vaccination or inoculation, or because their certificates are not on the prescribed International Form. Many travellers have been inconvenienced on this account and in some cases have even been placed in quarantine.

The onus of ascertaining the requirements of the country to be visited rests, of course, on the traveller, who should make careful inquiry of his travel agents or the consulate of the country concerned. The attention of medical practitioners, however, is specially directed to the following points, observance of which will assist travellers requiring certificates to avoid difficulties on their arrival abroad.

Smallpox.—A certificate of vaccination must be on the International Form which the traveller obtains from the travel agents and takes to his doctor. All headings on the form should be carefully completed in legible script. Both parts of the form must be completed—the second part after the result of the vaccination has been observed. Certificates only become valid fourteen days after the vaccination and normally remain in force for three years.

Cholera and Typhus.—Some countries demand certificates of inoculation against cholera or typhus or both. Here again the traveller must obtain the appropriate International Form and take it to his doctor. The certificate normally becomes valid six days after completion of the inoculation. In the case of cholera it generally remains valid for six months and in the case of typhus for not more than twelve months.

Enteric Fever.—Inoculation against typhoid and paratyphoid fever is seldom an international requirement and no International Form is prescribed for certificates of inoculation.

To obviate difficulties, the doctor's signature on any certificates which he gives to a traveller proceeding abroad should be authenticated by the town council, urban district council, or rural district council in whose area the doctor lives. The council will do this free of charge if the traveller takes or sends the certificate to them.

Yellow Fever.—Where inoculation against yellow fever is required the traveller can obtain it free of charge at any one of the approved centres named in the list set out in the "Notice to Travellers" issued at the Passport Office and the travel agencies. The centre will issue the necessary certificate on the prescribed International Form. It becomes valid ten days after completion of inoculation and remains in force for four years.

The Ministry of Health gives the following advice on the period which should elapse between smallpox vaccination and yellow fever inoculation: (1) Whenever possible, yellow fever inoculation should precede primary vaccination against smallpox. (2) There should be an interval of at least four days between yellow fever inoculation (when given first) and primary vaccination against smallpox. (3) If primary vaccination against smallpox is done first, there should be an interval of 21 days from the date of the vaccination before the yellow fever inoculation is given. (4) Where there is evidence of previous successful vaccination against smallpox, yellow fever immunization and revaccination against smallpox may be carried out at the same session, but if time permits yellow fever immunization should always precede revaccination by at least four days.

Western Union Agreement

The need for these certificates is not diminished, but the number of occasions on which travellers will have to produce them has been lessened by an agreement which came into operation on February 1. On that date the five countries of Western Union—Belgium, France, Luxembourg, the Netherlands, and the United Kingdom—became one single area for the health control of air traffic, and will henceforward be described administratively within the Brussels Treaty Powers as the "excepted area."

Regulations are being issued in each country to the effect that any aircraft which begins its flight at any place within the "excepted area" will not in normal circumstances be subject to health control on its arrival at any other place within the "excepted area." This does away with "Aircraft Declaration of Health" by the commander of the aircraft and with the "Personal Declarations of Origin and Health" by the passengers.

An aircraft bound for the "excepted area" which begins its flight outside that area, and the passengers, will be subjected to health control only at the first place of touching down within the "excepted area." The "excepted area" may be restricted by the Ministers of Health by public notice, to exclude temporarily any of the member countries or part of them in which there may be an epidemic.

This new scheme is the result of a system devised by the Public Health Committee of the Brussels Treaty Organization whereby existing control measures have been simplified without being impaired. Each country has furnished to the others particulars of all diseases notifiable in its territory, together with a list of its main airports and the names, addresses, and telephone numbers of the medical officers in charge with details of sanitary equipment at each airport. The same kind of "warning" postcard has been adopted for passengers landing from an "infected" area. They are advised to hand this to their doctor in case of illness developing shortly after their landing.

SPECIMENS FOR SEROLOGICAL TESTS

The Consulting Pathologists Group Committee of the British Medical Association has recently approved a memorandum on the submission of specimens for serological tests which was prepared by the Venereologists Group Committee. The memorandum is now published at the request of the latter committee.

Taking of Specimens

(i) *Blood.*—Blood should be withdrawn by venepuncture using preferably an all-glass syringe and needle sterilized by dry heat. The usual size of the needle is one with a 21 gauge, S.W.G. Dry heat is the best method of sterilizing. Boiling or autoclaving is permissible provided steps are taken to rinse in sterile saline solution. Spirit should never be used. A minimum of 5 ml. of blood should be withdrawn; the needle should be removed from the syringe and the blood allowed to flow gently into the blood container. Forcing blood through the needle must be avoided, because this damages the red blood cells, leads to haemolysis,[1] and also causes frothing of the blood, which interferes with the separation of serum from the clot. Blood can satisfactorily be withdrawn by means of a suitable hollow needle with rubber tubing attached.

In the case of infants, if venepuncture is impossible sufficient blood can be obtained by making a small incision on the heel with a sterilized Hagedorn needle or tenotome. This method is almost painless, and usually 1 ml. or more of blood can easily be obtained. If a specimen is sent through the post as serum it arrives in a condition that is better for testing than when sent as whole blood.

(ii) *Cerebrospinal Fluid.*—The cerebrospinal fluid should be allowed to drip into two small clean sterile containers which should be labelled "1" and "2." A total of 5 ml. (approximately 2 ml. in Tube 1 and the rest in Tube 2) is enough for routine purposes.

Labelling of Specimens

It is most important that confusion of specimens should be avoided, and block capitals should be used for names. It is recommended that the doctor should make out two labels giving *legibly* the patient's name or identification number. Rubber adhesive labels are most suitable. One label should be stuck on to the request form and the other on the tube(s) or bottle(s) containing the specimen(s). Before transmission to the laboratory, particulars on the specimen container(s) should be checked with those on the request form(s).

[1] The presence of haemoglobin in blood serum can make the reading of precipitation tests extremely difficult.

Clinical Information

The following clinical information should be provided as briefly as possible: (i) clinical summary; (ii) summary of treatment to date; (iii) results of last blood test; (iv) results of other tests (if relevant).

Sending of Specimens

Specimens should be sent to the laboratory as soon as is practicable. This applies particularly to cerebrospinal fluid, because any cell count is unreliable after two hours from the time the fluid has been obtained: it should not therefore be sent through the post. The sending of specimens over the week-end should be avoided, particularly during the hot weather. Bacterial contamination of cerebrospinal fluid renders it completely useless for serological tests.

Reports of Societies

FOOD FROM THE COMMONWEALTH

NUTRITION SOCIETY CONFERENCE

A conference on "Commonwealth Contributions to the British Diet" was held by the Nutrition Society in London on January 28, with Dr. W. K. SLATER, secretary of the Agricultural Research Council, presiding.

Canada and Australia

Colonel J. G. ROBERTSON said that since 1938 Canada had greatly increased her production of most foodstuffs, so that immense quantities of wheat, cheese, bacon, beef, apples, and salmon are now available for export. During the war about 4,000 million dollars' worth of foodstuffs were supplied to Britain either as gifts or on credit, and the only factor now restricting further supplies was Britain's inability to pay in dollars. The yearly production of wheat was now about 350 million bushels, of which 260 millions were available for export and 140 millions were actually exported to Britain. In 1944 Britain imported 657 million lb. of bacon from Canada, as compared with only 100 million lb. in 1949. Canada had nearly 50 million dozen eggs available annually, but this year the Ministry of Food had declined to enter into any contract to buy them. Despite the aid given by Canada to Britain since 1942 she now found that Britain would only buy her wheat and cheese, while going to Poland, Hungary, Russia, and Denmark for other foods which Canada would gladly supply.

Mr. A. H. HEYWOOD stated that last year Australia supplied Britain with 22% of her butter imports, 9% of her cheese, 10% of her processed milk, 7% of her eggs, 17% of her meat, 18% of her wheat, 100% of her oats, and 16% of her wine imports. Australia also provided more dried fruit than other countries, except Greece and Turkey, and helped with many foods, such as fruit juices, which lent variety to a monotonous diet. About 8 million Christmas puddings were supplied annually, and also about 3 million gift parcels. Meat supplies had been adversely affected both by a series of droughts, in which over 30 million sheep were lost, and by the very high prices now paid for wool; our imports remained below the pre-war level. Beef and pork production, however, should soon be considerably increased by the expansion of the scheme to grow sorghum grain in Queensland. The supply of poultry, which had now reached a level of 9,000 tons annually, was another promising development.

New Zealand and South Africa

Dr. C. S. M. HOPKIRK explained that in New Zealand the agricultural system was based on pasture, and that the two most important factors in limiting the productions of livestock and dairy products were labour and supplies of superphosphate fertilizer. The animal population comprised about 2¼ million dairy cattle, 2 million beef cattle, and over 32 million sheep. Since the production of grain did not even suffice for her human population, New Zealand could not compete with other countries in pig-breeding, but about 500,000 pigs were kept to use up skimmed milk and other dairy by-products. During 1948 Britain obtained 50% of her butter imports, 53% of her cheese, 17% of her beef, 65% of her lamb, and 77% of her mutton from New Zealand. The prospect of improving on these figures, by the eradication of diseases from livestock, by the use of more cattle to manure sheep country, and by increased mechanization, seemed very bright.

Mr. A. P. VAN DER POST gave reasons why the Union of South Africa was unable to supply Britain with any of the major foodstuffs and was only able to contribute items which might be classed as luxuries. For geographical reasons large areas of the Union were unsuitable for more than a low population of livestock. Wheat had to be imported, but maize, the staple food of the natives, was largely grown in the more fertile districts.

In sheep-farming the preference for the Merino breed provided excellent wool, but the quality of the mutton was too poor for export. Cattle were often used for draught purposes, and their beef would be unsaleable in Britain. The abundance of maize, which could be increased by the greater use of hybrid varieties, should allow the provision of bacon and eggs for Britain, and some progress in this direction had already been made. South Africa could also contribute oranges, apricots, peaches, plums, pineapples, and many other fruits. Sugar could also be supplied, but in varying quantities on account of frequent droughts.

Important contributions were also obtained from the surrounding ocean. Unfortunate experiences with snoek, associated with the less successful trials by certain canners when this fish was first available, should not discourage the British public from further trials of South African fish, which should not, however, be regarded as substitutes for salmon. Although two South African whaling ships were lost during the war, operations were now being continued with a modern German vessel which fell into Allied hands; after South Africa's demands have been satisfied the bulk of the oil thus obtained was supplied to the British Ministry of Food. The livers of many South African fish were being used extensively as commercial sources of vitamin A.

Mr. L. F. WIGGINS discussed recent trends in the sugar industry of the British West Indies. In 1948 Britain consumed about 2 million tons of sugar, of which about half was obtained from Cuba and other hard currency areas. An increase in the supplies from the West Indies would therefore both save dollars and help to raise the low standard of living of the native population there. The yield of sugar per acre could be increased by nearly 50% by the deeper cultivation of the Woodford-Lodge system, and losses might be avoided by combating insects, fungi, and the dangerous mosaic virus disease. Molasses, which still contained 30% of sugar, might be used for the production of rum, or of food yeast fit for consumption either by humans or by farm animals.

Overseas Food Corporation

Mr. N. R. FUGGLES COUCHMAN spoke on the work of the Overseas Food Corporation. The main purpose of the East African Groundnut Scheme was to provide oil to make good our shortage of fats, which had been caused largely by the cessation of supplies from India and China. Although we produced 45–50% of our requirements of some other foodstuffs we depended upon imports of oils and fats for 97% of our needs. Before the war our consumption was 60 lb. per head yearly; this had now fallen to only 49 lb. By clearing 3 million acres of bushland it was hoped to grow groundnuts equivalent to 250,000 tons of oil.

Financial limitations combined with unfortunate weather conditions, however, recently necessitated the reduction of the area to be cultivated to only 500,000 acres, with a corresponding fall in the expected yield of oil and a delay in completion of the scheme until 1954. It had also been found desirable to grow oil-yielding sunflowers in addition to groundnuts, and the cultivation of soya beans was under consideration. The Corporation's scheme in Queensland had proved more straightforward. Old ranching properties, in which the pasture had been impoverished by overgrazing, were taken over for the

production of sorghum. This crop would be used partly to fatten cattle, but the grain would be either sent to Britain for use as fodder or consigned to large piggeries which would be erected in Queensland in irrigated areas near the coast.

Dr. J. HAMMOND, F.R.S., stated that before the war Britain imported 40% of her meat supplies, but that the reorganization of our agricultural policy to produce more cereals and milk had now raised our meat imports to 55%. During the war quality was neglected, but poor, tough meat was again becoming difficult to sell. Supplies of home-produced meat in Britain were lowest between January and July, and, while our storage accommodation remained inadequate, additional imports from Australia and New Zealand during this period would be helpful. Caution was necessary in importing meat from the Continent on account of the danger of spreading foot-and-mouth disease, while imported poultry might introduce fowl pest.

Dr. A. GREEN commented on the wide variations in composition between different strains of wheat. Canadian wheat is much richer in protein than either British or Australian wheat. Wheat rich in protein was essential for baking good bread and desirable for nutritional reasons.

Bacon and Fruit

Dr. E. C. CALLOW explained that in 1938 we consumed nearly 11 million cwt. of bacon, of which 22% came from the Commonwealth, including 1¼ million cwt. from Canada and half a million cwt. from Eire. In 1949 our consumption was only 6 million cwt., of which 18% came from Commonwealth sources, including slightly under 1 million cwt. from Canada and only 24,000 cwt. from Eire. Substantially increased supplies from Australia were now anticipated as a result of the Queensland scheme.

Dr. R. G. TOMKINS said that while in 1936 we consumed 84 lb. of fruit per head annually, of which about one-quarter was home-grown, in 1947 we consumed 76 lb., of which half was home-grown. Our reduced imports of oranges could be explained partly by decreased production in the countries supplying them. In continuing the present tendency towards a return to our pre-war pattern of fruit consumption we might contemplate importing apples from New Zealand; apples, dried apples, and fruit pulp from Canada; fruit juices, tomato juice, and fruit cakes from Australia; and grapes, deciduous and citrus fruits, canned fruits, and fruit juices from South Africa.

Dr. E. CAPSTICK pointed out that our butter consumption was now only three-fifths of the level before the war, when we used to obtain large quantities from countries now behind the "iron curtain." Our cheese consumption, however, had increased by one-third, while our decreased use of condensed milk had been balanced by an increased use of dried milk. It seemed highly desirable that Canada, Australia, and New Zealand should send us cheeses to suit all tastes, and should not always concentrate on the familiar Cheddar variety.

Mr. C. H. CLARKE discussed our supplies of edible oils and fats, which were derived mainly from Commonwealth sources. The palm tree was in many ways superior to the groundnut in providing fat, but took much longer to mature, and required different climatic conditions.

Mr. P. LYLE emphasized the need for increased sugar production in the West Indies both in order to satisfy Britain's requirements and to provide for the rapid increase in the native population, which in Jamaica might be doubled during the next 35 years. By growing yeast on sugar-cane juice it should be possible to obtain very high yields of protein per acre, yields equivalent to a population of about 20 bullocks per acre. The present high price of food yeast was due to the small demand, which meant that a factory with an expensive permanent staff could not be kept working continuously.

In summarizing the day's proceedings Dr. SLATER suggested that lack of labour was the main factor limiting the production of food in the "empty spaces" of the Commonwealth. A solution of both our nutritional and economic difficulties might be found if more workers could be persuaded to take up employment in agriculture, while those left in industry could be urged to increase their efficiency so as to maintain production at its present level.

Correspondence

Fifty Years of Medicine

SIR,—I am sure that everyone who has read through the distinguished company of writers in your "Fifty Years of Medicine" (January 7, 1950) has found great pleasure and a renewed interest and orientation on how and why we are where we are to-day. As a record of the fascinating synthesis gathered together and presented in such a pleasant form our successors in a further fifty years will not fail to read into it some vivid character studies of the particular essayists. We hope that they will be able to picture the noble group as we now know them. May I suggest, Sir, that this volume of the *British Medical Journal* be published in book form? I can think of nothing better as a presentation piece to a senior clinical student or even to a junior registrar, and for most of us a re-reading once a year might give a modicum of balance in aid of reasonableness towards the rapid advances in factual knowledge and mould our philosophy to the changing scene.

One hesitates to offer a word of criticism, but I think there is an omission. There is singularly little concerning the child. It might have been a happy thought to have included an essay on "The Child in Health and Disease." I need hardly mention the talented writers who could have dealt with this, and no doubt an opportunity would have occurred for some commemorative notes on the great advances in social, mental, and physical paediatrics and the strength of our present-day outlook in child health. The writer might have reflected somewhat upon such great pioneers of the past fifty years as—let us mention an unselected few—L. G. Parsons, K. D. Blackfan, W. K. Marriott, C. McNeil, F. Still, A. Wallgren, and T. Barlow.

Happily there are a few scattered remarks in some of the essays, but I feel that from the historical standpoint the extreme interest and great achievements in the study of infancy and childhood in the past fifty years are most inadequately represented.—I am, etc.,

Bristol. A. V. NEALE.

SIR,—Reading your "Fifty Years of Medicine" (January 7, 1950) I noted with dismay that while the advances made during the past half-century in every other of the branches of surgery were fully dealt with, those which have been achieved in gynaecological surgery received no mention at all, though they have been as important as any in the whole realm of surgery.

Remembering, as I do, the number of splendid men who in the last fifty years have laboured to that end, this omission goes to my heart and confirms the fears I have expressed many times in the past, that the divorcement of gynaecology from surgery in general would be disastrous to the specialty. The science and art of gynaecological surgery was initiated by general surgeons in this country, and all its most striking advances up to the present time have been made not by pure specialists but by men whose interests in surgery were wide.

I have always held that obstetrics (but not paediatrics) was basically a surgical art, to be regarded simply as one department of gynaecology, and my object in 1926 in becoming a candidate for the Council of the Royal College of Surgeons was to bring gynaecology, and with it obstetrics, under the undisputed aegis of surgery. Events, however, defeated me: the separation I tried to avert took place, and for many years I refused to join those responsible for it on the ground that the step they had taken was not in the best interests of the specialty. The absence of any mention of gynaecological surgery in your important review confirms the justice of my prognostications and makes me very sad indeed.—I am, etc.,

London, W.1. VICTOR BONNEY.

Fate of the Foreskin

SIR,—Dr. Douglas Gairdner's article (December 24, 1949, p. 1433) is remarkable not only for the kind of information it supplies but for the restraint with which he makes the plea that we should desist from circumcising our male infants except when certain well-defined conditions compel us. He was wise to refrain from invective, for this is a subject about which convictions or beliefs are strong and in which reason plays little part. Irony in plenty is to be expected in these correspondence columns, but he remains above our level, and his resisting this temptation will be rewarded, I am sure, by his article having a greater influence than if it had been more provocative.

May I before this correspondence closes bring forward another argument against circumcision which, though never given serious consideration by doctors, seems to me to be just as valid as the demands of ritual or the various prophylactic reasons offered on the other hand. I mean the aesthetic difference between the natural and the circumcised state. Dr. Gairdner mentions as one of the possible minor advantages of circumcision "the supposed aesthetic or erotic superiority of the shorn member," but for want of enough evidence does not discuss this point. I do not wish to confuse the erotic with the aesthetic. I refer here only to the form, not the function, of this member, and I appeal to those who find aesthetic pleasure in the form of the human body—especially in the beauty of children. The child's whole body and limbs, though relatively formless, are a joy to contemplate. It was unthinkable to Donatello or Michelangelo to represent David bearing the mark of his religion and race, though they did not spare him many an awkwardness and imperfection of youth. Why should our respect for what is right or wrong in the human body be any different from theirs?

Circumcision at the best is a slight disfigurement and at the worst, as we have all seen, a mutilation. Let disfigurement be accepted by all means as part of the sacrifice in ritual circumcision, but why should it be tolerated when there are no such solemn motives but only vague fears on the part of parents that the infant with an intact foreskin has troubles ahead? And why should doctors, who normally take pains to minimize any disfigurement of the body, continue to justify this particular one to parents and to one another in the name of various prophylactics, including that far-fetched bogy the risk of carcinoma of the penis? Surely if we are to carry prophylaxis to this extreme the next step should be false teeth for everyone at the age of 30 as a safeguard against cancer of the tongue. I appeal to readers of this letter to consider all future decisions about circumcision with their aesthetic senses awakened.—I am, etc.,

London, W.C.1. DERMOD MACCARTHY.

SIR,—During 1946–7 I made a point of asking all mothers of circumcised children attending a London borough toddlers' clinic why the operation had been undertaken. The reasons given, in numerical order, were these: (1) advised by doctor, usually because of an unretractable prepuce at birth; (2) advised by nurse or midwife; (3) desired by father; (4) family custom ("all mine have been done"); (5) religious reasons in Jews and Moslems.

Clearly in this particular sample the main factor in promoting circumcision is medical advice. I asked a few nurses and midwives to give me an idea of the conditions which they regarded as indications for circumcision. The reasons given were adherent prepuce at birth, cleanliness and ease of washing, and, rather surprisingly, the idea that circumcision "prevents masturbation" (two subjects). Even if the factual inaccuracy of this suggestion could hardly be missed by a circumcised father, the implication it carries may well continue to play a part in determining parental attitude, at least until teaching on normal sexual development in the child becomes more insistent and explicit.

The reasons which caused fathers to advocate the circumcision of their sons had to be obtained at second-hand via the mother. They included cleanliness (probably influenced by the idea of venereal disease prevention), the fact that the father was himself circumcised, and the statement that it is "better for the woman." Parents in primitive cultures show great zeal in transmitting to children of their sex the benefits of any ritual mutilation they themselves have undergone, even when, like female circumcision in the Sudan, it is a painful affair and a life-long handicap. It would be unwise to theorize about the sociology of circumcision in England or its unconscious motives, if any. It does, however, seem clear that it would decline without active medical support, much of which is to-day based on the anatomical error which Dr. Douglas Gairdner (December 24, 1949, p. 1433) exposed. It is quite possible that even in new-born infants operation, and particularly operation in hospital, can produce psychological trauma, though the same operation delayed into the genital phase would probably do much more harm. We do not, however, need to rely on any mental-health argument to deter us from unnecessary surgery.—I am, etc.,

London, S.E.23. ALEX COMFORT.

SIR,—May I make three comments on Dr. Douglas Gairdner's excellent paper (December 24, 1949, p. 1443)? First, he puts the age at which retractability should be attained at 3 years. In my opinion, this is too young. Many perfectly normal boys still have incompletely separated prepuces up to the age of 6 or 7, and eventually separation occurs normally. At 3 years there is nearly always some organic union between the glans and the overlying skin, and forcible separation at this age is a painful and terrifying process.

Secondly, circumcision may predispose to enuresis. Of boys attending the enuresis clinic at the Leicester Royal Infirmary 37% are circumcised, while only 29% of 200 non-enuretic boys of the same age and class have undergone the operation. Lastly, when medically supervising boys of 5–15 years of age in a children's home I have found that those with a low intelligence quotient fail to keep their prepuces clean and are prone to balanitis. I believe that boys of this type should be circumcised. In fact, circumcision should be confined to the dull, the dirty, and the brutish. The intelligent, the cultured, and the cleanly should be allowed to keep their foreskins.—I am, etc.,

Leicester. J. VERNON BRAITHWAITE.

Myoidema

SIR,—Drs. G. F. Taylor and P. N. Chhuttani (October 8, 1949, p. 784) have attempted to boost the value of "myoidema" as a sign of clinical significance when it was happily and deservedly falling into disrepute. Dr. J. H. Jackson has supported their contention in a letter (November 26, 1949, p. 1232). It may be remembered that there has been great difference of opinion about the significance of the test in the past. West[1] and many others regarded the sign as of little value in the diagnosis of any one disease, as it frequently occurred in a wide variety of conditions, and suggested that it might be physiological. I write to confirm the suggestion.

My attention was particularly drawn to this sign a few years back, when after demonstration of the clinical sign to the students in the wards, followed by the stereotyped explanation that it suggests wasting disease, tuberculosis, or avitaminosis, one student after another came up to me manifesting great discomposure at the presence of the sign in himself. I found that both "fascicular" and "nodular" contractions were observed in them on mechanical stimulation. The students were, and still are, in excellent health. This incident modified my views about the significance of the sign, and on subsequent occasions while referring to it during clinical teaching I mentioned it to be of no clinical significance.

After reading the article by Drs. Taylor and Chhuttani I again examined thirty persons, consisting of medical students and nursing staff, all in excellent nutritional condition and health. Both the "fascicular" and "nodular" contraction tests were done on them in the lying-down position, following the technique described in the paper: only in three female subjects could the "fascicular" contraction test not be elicited. In all the other subjects both the tests were positive. I would

attribute the negative tests obtained in the three female subjects to the adiposity of the chest wall.

The "biceps-pinching" test to elicit myoidema reminds me about a trick which I and my friends played on each other in my childhood. The trick consisted of biceps pinching as described in the paper, and bringing out a nodular swelling which we used to call then a "toad" or "frog." In the case of a muscular boy some strength and skill were required to bring out the "toad" in his biceps. I was supposed by my friends to be expert in bringing out the "toads" in boys in whom it refused to appear by the efforts of others. This recollection further convinces me about the purely physiological nature of myoidema.

The writers attribute the unfavourable opinion about the significance of myoidema to the mistaken synonymous use of the terms "muscular irritability" and "myoidema"—which respectively mean "fascicular" and "nodular" contraction on mechanical stimulation of the muscle. To me this distinction appears to be more quantitative rather than qualitative, depending upon the strength of the stimulus and the size of the muscle strands. Whereas myoidema can be elicited with some skill and by varying the strength of the stimulus in almost every person, muscular irritability is sometimes difficult to obtain in the obese and the thickly set. In conclusion, I am of opinion that myoidema as described in the paper and also muscular irritability are both physiological phenomena and have no pathological significance in clinical examination.—I am, etc.,

Sassoon Hospitals, Poona, India. P. L. DESHMUKH.

REFERENCE

1 West, S., *St. Bart's Hosp. Rep.*, 1879, **15**, 151; *British Medical Journal*, 1949, **2**, 274.

Actinomycosis

SIR,—The theory that the source of actinomycotic infection in man is grass or straw is no longer tenable. The publication of Mr. Zachary Cope's Bradshaw Lecture (December 10, 1949, p. 1311) has prompted me to record the following case.

A lad of 15, employed as a farm worker, was admitted in 1941 to Addenbrooke's Hospital under the care of Mr. V. C. Pennell. Five weeks before admission he had noticed a painless swelling on the left side of his face, which had increased slowly in size. On examination, he had a tumour about the size of a walnut situated in the region of the left parotid gland. It was tender on palpation and thought to be fluctuant. The overlying skin was slightly reddened, but the patient was apyrexial. A clear secretion could be expressed from the parotid duct. As the swelling was increasing in size it was felt that exploration was indicated. At operation, the superficial tissues were oedematous, and the swelling was found to be lying in the substance of the parotid gland. Further dissection resulted in the escape of about 5 ml. of yellow pus containing "sulphur granules." On exploring the abscess cavity a grain of barley was discovered with two husks. Laboratory examination showed that streptothrix was present in a film of the pus, and a "growth of filamentous organism, probably actinomyces," was produced on anaerobic culture. A section of the parotid gland examined histologically showed granulation tissue. On subsequent careful questioning, the patient remembered that while harvesting he had been in the habit of pulling off handfuls of barley, which he chewed, spitting out the husks.

It seems certain that in this case the barley grain had entered the parotid duct, carrying the infection from the mouth to the gland. Similar cases have, perhaps, formed the basis of the "traditional and popular fairy tales about infection from grass or straw" to which Mr. Zachary Cope refers. But, as he points out, they should now be put aside in the light of modern knowledge of the actinomyces.—I am, etc.,

Cambridge. J. F. R. WITHYCOMBE.

Dangers of Dicoumarol

SIR,—The dangers of dicoumarol as described by Dr. H. Lempert (January 21, p. 183) are very real. The benefits of dicoumarol are also very evident even if less dramatic. Careful supervision of every case is essential.[1] I find the method of prothrombin estimation which employs "stypven" with or without lecithin quite satisfactory. We have had no haemorrhagic complications in our cases since 1945, when we first started using dicoumarol. Good technique is essential both in the laboratory and in the wards. Given good technique, there is no danger to the patient. Casual or careless technique causes casualties.—I am, etc.,

Epping, Essex. FRANK MARSH.

REFERENCE

1 Marsh, F., *British Medical Journal*, 1946, **2**, 963; 1947, **2**, 748 and 1009; 1948, **1**, 319 and 1207.

Multiple Ectopic Pregnancy

SIR,—I have read of bilateral ectopic pregnancy, but I imagine triplets must be rather rare, which is my only reason for publishing this case.

On December 4, 1949, a married woman aged 27 was admitted to Margate General Hospital under me as a case of ruptured ectopic gestation. She had one child aged 7. She gave a history of normal menses till the last period, which started on September 11 and lasted five days. On October 5 she had a slight blood loss from the vagina and then commenced to have pains in the lower abdomen of which she took little notice. During November she had frequency of micturition and dysuria, for which she received treatment. Since the third week of November she had occasionally vomited slightly.

On December 4 at 1 p.m. she was seized with sudden generalized abdominal pain, worse in the hypogastrium. There was no bleeding per vaginam. She was not seen by her own doctor until about 7.30 p.m., when she was at once sent in to hospital. On admission her pulse was 84, temperature 99° F. (37.2° C.). There was generalized abdominal pain, worse below the umbilicus, where there was tenderness and moderate guarding, but no abnormal mass was palpable. Vaginal examination revealed tenderness, but no bleeding. Her face and lips were pale.

At operation a paramedian incision below the umbilicus was made and a large quantity of blood clot found and removed. The uterus was a little enlarged. The left tube, from which a firm ectopic mass—approximately 1¼ by 4½ in. (3.75 by 11.25 cm.) in size—was almost completely extruded, had ruptured into the broad ligament and bled freely. This tube and ovary were removed. The right tube was inspected and found to be adherent to the floor of the pelvis by an organizing blood mole projecting from and distending the distal half of the tube, which was then removed. The wound was closed without drainage, and the patient made a good recovery, leaving hospital on December 18.

The mole contained in the right tube consisted of organized blood clot with no traces of the embryo, but that from the left tube when opened was found to contain an unruptured amniotic sac containing uniovular twins aged approximately five weeks.

—I am, etc.,

Ramsgate, Kent. A. J. K. DREW.

Brachial Plexus Block

SIR,—It was with interest that I read the article by Dr. S. V. Humphries (January 21, p. 163) reporting his experience in 350 cases of brachial plexus block. I published my original paper on the technique of brachial plexus block in 1940.[1] The essence of the technique was that a sector of tissue lying between the mid-clavicular point on the skin and the first rib was uniformly infiltrated with some 60 ml. of 2% procaine–adrenaline solution. I advocated starting the injections lateral to the plexus and slowly working medially until the subclavian artery pulsations transmitted along the needle indicated that the lower trunk of the brachial plexus had been reached.

This technique was taken up by Macintosh and Mushin, who published their book[2] in 1944, and it is to their credit that the procedure has become so popular. They modified the technique, however, by starting the injections of procaine into the lower trunk of the brachial plexus close to the subclavian artery and working laterally.

It sometimes takes several proddings with the needle before first striking the surface of the first rib, especially in its more anterior part, where the needle approaches it at an acute angle. Once the surface of the rib has been located with the point of the needle it is comparatively easy to reach it at each successive injection. It seems wrong to me, therefore, to make the first injection into the medial part of the plexus, as advocated by

Macintosh and Mushin, for, in probing for the first rib here, each unsuccessful insertion of the needle damages the plexus to some minor extent. Surely it is wiser to sound for the first rib with the needle well lateral to the plexus. The first rib can often be easily palpated at this part, and it exposes a broad flat surface normal to the line of the needle at this point. If more than one probe has to be made before striking the rib one knows that no vital structures are being transfixed in this area.

Brachial-plexus-block anaesthesia following my technique, or Macintosh and Mushin's modification of it, has been used for some years by many anaesthetists and surgeons. Humphries's figures coincide with my own and the results of the Oxford school. Is this the general experience? Complications following plexus anaesthesia seem singularly rare, but it would be interesting to know if any serious complications have been encountered by others, particularly evidence of injury to the plexus. I have always avoided using it in septic conditions, but I wonder if my aversion to its use in such cases is justified.

It would also be of interest to know what modifications of the technique have been adopted by others. I originally used some 60 ml. of procaine-adrenaline solution simply because I found such a large volume in an adult safe, and I considered too large a volume more likely to be successful than too small. I have no doubt, however, that those anaesthetists who have now a much greater experience than I have found a smaller volume of a more dilute solution adequate.—I am, etc.,

Glasgow. JAMES PATRICK.

REFERENCES

1 *Brit. J. Surg.*, 1940, **27**, 734.
2 *Local Anaesthesia : Brachial Plexus*, 1944, Oxford.

SIR,—Dr. S. V. Humphries's observations (January 21, p. 163) on brachial plexus block are both informative and interesting. It is, as he says, a very valuable and inexpensive form of anaesthesia (and safe). The parentheses are mine, because three years ago I was asked to remove the broken end of a needle which snapped in the supraclavicular triangle while the plexus was being infiltrated, using the Macintosh and Mushin technique. I was in the theatre at the time of the mishap and proceeded to remove the needle without altering the patient's position or using any more anaesthetic.

An incision 3 in. (7.5 cm.) long, centred over the injection site, was made parallel to the clavicle. The track of the needle was followed down to Sibson's fascia, when the protruding end of the needle was located with the tip of the index finger. Further dissection and retraction exposed the needle, which was seen moving on respiration, on the medial aspect of Sibson's fascia. It was ultimately retrieved with some difficulty from its precarious position.

The patient made an uneventful recovery, but the anaesthetist and I had an anxious fifteen minutes.—I am, etc.,

Liverpool, 7. R. MARCUS.

Analgesia in Childbirth

SIR,—Dr. C. Langton Hewer states (December 31, 1949, p. 1521): "More recently pethidine and physeptone have been employed, but unfortunately all these drugs tend to diminish uterine contractions and to depress the infant's respiration." I have read well over forty papers on pethidine dealing with approximately 20,000 pregnancies, and the experience of the authors of these papers differs from that of Dr. Langton Hewer. For example, Carter[1] reported on 2,700 cases on which he had used "a brand of pethidine" as follows:

"There is no respiratory depression, there is no asphyxia of the newborn from too much analgesia of the mother, there is no increase in the usually small number of slow-to-breathe, full-of-mucus babies. From the local observations in over 2,700 cases I feel that we are nearer than ever before to an ideal analgesic method in obstetrics and that 'demerol' hydrochloride (pethidine) in combination with scopolamine or some other drug is not surpassed by any other drug or method which has to date been administered or has been in common use."

In England, Barnes[2] thus described her results in 500 cases of pethidine in labour: "It may be concluded that pethidine approaches the criteria for an ideal analgesic for use in labour more than any other known substance. Its chief advantages are safety, lack of toxic effects, lack of effects on the course of labour, and simplicity of administration." Roberts[3] discussed pethidine in combination with scopolamine and concluded that since the introduction of pethidine and scopolamine in the obstetric department of her hospital there has not been an increase in the foetal mortality. In cases of foetal morbidity the cause could not be attributed to the analgesia given during labour. From analysis of her figures showing effect on the length of the first and second stages she says: "Thus there is a suggestion that pethidine and scopolamine in fact have the effect of shortening labour if anything." She gives tracings of the action on uterine contractions, and writes, "There did not seem to be any alteration of rhythm or amplitude."

Emlin,[4] in a report on 5,000 consecutive deliveries without a maternal death due to pregnancy, describes his routine sedative as 100-mg. doses of pethidine given intramuscularly. Scott and his colleagues[5] showed by experiments on animals that pethidine had a stimulating effect on respiration. All other substances except one in the series tested caused depression of respiration.

At a time when every effort is being made to improve analgesia in childbirth I think it important that these facts should be brought to light to correct the impression which Dr. Langton Hewer's article gives, since readers taking it to heart might refrain from using the drug and thus deprive many women in labour of what is described as "a safe, non-toxic, and efficacious substance."—I am, etc.,

Welwyn Garden City, Herts. F. WRIGLEY,
Director of Clinical Research,
Roche Products, Ltd.

REFERENCES

1 *Wisconsin med. J.*, 1945, **44**, 1170.
2 *British Medical Journal*, 1947, **1**, 437.
3 Ibid., 1948, **2**, 590.
4 Ibid., 1949, **1**, 260.
5 *Science*, 1946, **104**, 587.

Animal Experiments

SIR,—In the annotation (December 31, 1949, p. 1518) upon this subject you make a statement which is, I think, so mistaken that it greatly weakens your case, with which, in general, I am in agreement. You say that no good reason exists for making a distinction between dogs and other animals, such as rats. The dog, like man and certain other higher animals, has personality—that is to say it can make, in some degree, personal relationships. Animals such as the rat, which cannot do this, are very properly regarded as lower, and this is an important distinction. The dog is able to regard a man, in some degree, as a friend or an enemy, but a rat can only appreciate a human being as a source of food or a source of discomfort. There are indeed other arguments for not exempting dogs as experimental animals, but the one you give is not, I feel, a valid one.—I am, etc.,

Cambridge. C. G. EASTWOOD.

Treatment of Varicose Veins

SIR,—I feel I would like to continue my long-range correspondence on this subject and to reply to Dr. Hanschell's letter (October 22, 1949, p. 932). There are certain matters in this letter that are not strictly concerned with the treatment of varicose veins and that call for comment first. The repetition of the phrase "of course" is called provocative. On rereading my letter I agree, and can only assure Dr. Hanschell that this was not intentional but the result of poor composition. He has, moreover, rubbed it in with vigour in his reply, so I am happy to cry quits. Dr. Hanschell is right when he supposes that I more than glanced at Sir Heneage Ogilvie's article (September 24, 1949, p. 665), and I agree that he damns with restraint—an admirable quality seen in all his writings.

Now as to the treatment of varicose veins, I have reread Dr. Hanschell's letter (March 19, 1949, p. 500) and agree that his original statement was "Sclerosant injection is dangerous or useless," and not "and useless." However, I have always understood that he meant that an injection that was strong enough to be of use was, at the same time, dangerous, and,

vice versa, that an injection weak enough to be safe was useless. With this I still entirely disagree, and maintain that the dose and strength of the injection can be so regulated that it can be effective without prolonging convalescence and without being dangerous. This statement is based on experience and observed facts, not theory. My first letter (March 5, 1949, p. 412) dealt with Boyd and Robertson's views on the danger of retrograde injection, based on phlebographic evidence. I did not consider their evidence sufficient to warrant discontinuance of such injection, nor do I consider Dr. Hanschell's evidence sufficient. An accident from an operation can result from the unskilled application of a principle and not from the principle itself.—I am, etc.,

Sydney, Australia. C. H. WICKHAM LAWES.

*** This correspondence was closed on December 31, 1949, but we are publishing Mr. Wickham Lawes's letter because the *Journal* is not received by readers in Australia until some weeks after publication in this country.—ED., *B.M.J.*

A Scientific Society

SIR,—Lord Russell's exposé of our planetary plight in his Lloyd Roberts Lecture (December 10, 1949, p. 1307) is not matched in impressiveness by the solution he offers—namely, food and birth control to be planned and enforced by a world authority. Almost the whole of the section entitled "Psychological" is a weighty argument against the forced optimism of his penultimate sentence—"But, while upheavals and suffering have hitherto been the lot of man, we can now see, however dimly and uncertainly, a possible future culmination in which poverty and war will have been overcome, and fear, where it survives, will have become pathological." If this conclusion, with its triple hedging of the bet, carries to any reader an impression of more than forced and verbal escape from gloom I am only saying I am surprised. I doubt if the speaker himself feels any optimism at all.

In passing, it is difficult to see how the conception of fear as pathological can stand in a paper that purports to include biology in its subject-matter. This and other examples of unrealism throughout the address are disturbing when they come from one who speaks with Lord Russell's authority. How differently wrote the young author of *Roads to Freedom.*

The goal of mankind is happiness: all philosophers are agreed about that. Happiness is displayed in nothing so much as in spontaneity. That some world authority is going to give us happiness by "planning" down to the most intimate details of our lives—e.g., sex life—and by destroying spontaneity there, is a clear contradiction in terms. This is what logical positivism leads to. One of the most common symptoms of a common mental sickness—some call it the anxiety neurosis—is a tendency to over-plan, an obsession with the incalculable future, and an attempt so to order it in the mind that a false escape from present maladjustments is phantasied. The parallel with our sick society is close: the plethora of planners would be intolerable to common sense if they did not often cancel one another out. (For instance, the Food and Agriculture Organization cries for more artificial fertilizers, and Lord Russell and Mr. Aldous Huxley cry out against them. We cannot have both A and not A.)

What common sense does is to mind its own business, the business of the day before it. The business of our leaders is the immediate future and not possible future culminations. Nearly every human problem can be solved by beginning to solve it; otherwise human life is ultimately meaningless. If indeed Lord Russell believes it to be so it would be better that he should say so outright. The plain man sticks to fundamental duties and rights. Like Candide and the Arab whom Lawrence met in the oasis, he tills his own garden, and he does not concern himself with whether his neighbour (much less the Central African) is having too few children, or too many, or somebody else's. The eyes of a fool are on the ends of the earth. After all, we have got certain fundamental rules to guide us, and these are surprisingly common to all races and creeds. Planners of Lord Russell's type are in danger of neglecting these to the ultimate confusion of our civilization.

Bad workmen blame their tools. It is characteristic of some Utopia-mongers that they want to lay the blame on the bricks. They want to make man into something quite unrealistically different from what he is. They want all men to be equal and, what is even less realistic, to behave as if they were. Ignoring the clamant facts of our mortal lot, they prophesy abolition of poverty and sickness. The final absurdity came from Mr. Bernard Shaw when, in *Back to Methuselah,* he suggested that we might live for ever or as near to it as is no matter. They want to abolish fear, though when they write as psychologists in the very same essay they admit that fear adds spice to life and is sought for by young men who play rugger and old men who climb the Matterhorn. They have for long enough wanted to rationalize our food and have succeeded in rationing it so as almost to destroy the pleasures of the table. Alcohol (by which they mean good beer and good wine) have almost gone, except for the very rich or those who are so highly placed in bureaucracy as to be beyond controls. Now they want to ration our loves. All these things are remotely possible, and some of them are already coming to pass. But do not let us pretend in the applause-catching optimism of a curtain paragraph that they will make for the happiness of mankind.—I am, etc.,

Edinburgh. A. G. BADENOCH.

SIR,—Bertrand Russell's lecture to the Royal Society of Medicine in November (December 10, p. 1307) illustrates even more clearly the way in which certain Western philosophers are building up a new ideological background to justify their hatred and fear of all those social developments now taking place in Eastern Europe and Asia. The scare of over-population and their cry for drastic birth control re-echo only too plainly the arguments put forward by William Vogt in his book *Road to Survival*—a book which deals with the world problem of soil erosion and which is reputed to have thoroughly unnerved many influential people in the United States. The argument that "malaria is a blessing in disguise" and that "the tsetse fly has actually been a protector of important resources" are all to be found in Vogt's book, and Bertrand Russell's idea of a beneficial Black Death in modern dress is only a further step in this dangerous philosophy.

His "explanation" of the victory of communism in China is even more illuminating: no less is his vision of the future with "blocs in which the hungry nations band together against those that are well fed." He sees no hope of the well-fed nations helping the hungry ones; neither, for that matter, does Mr. Vogt, who goes so far as to lay down conditions for the small amount of help which the well-fed nations may choose to give.

> "Anything we (in the United States) do to increase the population is a disservice both to Europe and ourselves. We are in a position to bargain, and any aid we give should be made contingent on national programmes leading towards population stabilization. . . . And as we pour in hundreds of millions of the American taxpayers' dollars we should make certain that substantial amounts are available for educational and functional contraceptive material."

Bertrand Russell's philosophy is of no use to us, and to any readers who would like to have some of this "intellectual dead wood" cleared away I would strongly recommend that they buy and read *Man against Myth,* by Professor Barrows Dunham, for this is a book to inspire confidence in the future of the world.—I am, etc.,

Halifax. M. N. TEMPEST.

Prognosis in Disseminated Sclerosis

SIR,—The assessment of the prognosis in disseminated sclerosis may be one of the most important factors in dealing with young patients at an age when careers and marriage are of the greatest moment and must be discussed in relation to the disease as part of the problem. It is usual for the patient to be given a very guarded and the relatives a pessimistic prognosis, and certainly Dr. Margaret Reinhold's (January 21, p. 160) work supports this point of view. She states her difficulty in obtaining material for her review except from the hospitals for incurables and the National Hospital, which cater for those patients who have deteriorated until helpless or who have some

unusual features in the disease. They are all in the most severe class of case.

It would be of very great value if some comparable survey could be made of patients suffering from disseminated sclerosis who remain in their own homes. It would be admittedly a very difficult business, but I believe it would be of the greatest interest to know the extent of the more benign types of the disease. There are many patients who have very long remissions with many years of no disability, and some of these do not relapse. If there were any way of knowing this early it would save much mental suffering.—I am, etc.,

Leicester. JOAN B. WALKER.

Safe Medical Terms

SIR,—Dr. A. Wynn Williams (January 14, p. 102) has done a very good piece of work which will enable clinicians to use the term "gastritis" more intelligently. But I wish he had not called his fixative "formol-saline." Maybe this is all right in the laboratory, but it may be dangerous when it finds its way to the theatre or wards. Not all nurses have keen senses of smell and hearing, and I know one instance of a student nurse who mistook formol-saline for normal saline, with disastrous results to the wound she irrigated. I would prefer a safer term such as "salt-formalin" for the laboratory fluid, and the unambiguous term "physiological saline" instead of normal saline for the wards.—I am, etc.,

Enfield, Middlesex. C. ALLAN BIRCH.

Virus Theory of Cancer

SIR,—In a leading article (December 31, 1949, p. 1516) it is remarked that the somatic-cell-mutation theory of tumour formation is "pure speculation," and a similar observation is made by Dr. C. H. Andrewes (January 14, p. 81). I make no comment on these expressions of opinion except to ask how, in the event of a tumour being actually produced by a virus, it is proposed to explain—and this exactly and in detail—first the production and then the transmission to descendant cells of the specific newly developed characters of the tumour cell otherwise than by an appropriate alteration of the gene mechanism which controls cell formation and division.

There are only four cases of importance in which it has been alleged that a virus is the cause of tumour formation. These are the Rous sarcomata in fowls, Lucké's adenocarcinoma of the kidney of the leopard-frog, Bittner's mouse mammary carcinoma, and the Shope papilloma of the cotton-tail rabbit. In only one of these, the Shope papilloma, has it been shown that a virus produces the condition, and in this case the virus disappears when the papilloma, a benign growth, becomes malignant, as it frequently does in the domestic rabbit. Dr. Andrewes has not been very successful in the attempt in his article to dispose of this difficulty, which, I would emphasize, is a very crucial one.

A few remarks on another of the four cases, that of Bittner's mouse mammary tumour with its "milk factor," would not be out of place in the present context. Such tumours make their appearance occasionally in isogenic inbred strains of mice, and such a growth can subsequently be maintained indefinitely in the strain in which it arose. The process of inbreeding is well known to render patent hitherto latent and harmful recessive characters, and it is highly probable that this is what has occurred here, the result being the appearance of the tumour with its so-called milk factor. Of course every case of inbreeding does not produce such a condition: indeed this occurs rarely, and accidentally so to speak, while the milk factor, having arisen in the mammary secreting cells, is passed on in the milk to affect similar cells in the descendants of the animal in question. The production of tumours by the milk factor is conditioned by isogenicity of the mice, by its action on a specific tissue cell, that of the mammary gland, which arises in development through appropriate changes in this isogenic genotype, and by oestrogenic stimulation.

One can envisage here a situation where recessive genes in control of an injurious hormone replace dominant genes in control of one which normally, in conjunction with pituitary, adrenal, and ovarian hormones, is active locally in the very intensive metabolic and catabolic processes taking place inside the milk-secreting cell. In this context it is significant that for the production of the factor the fully differentiated milk-secreting cell is necessary, and that for the exhibition of its optimum effect—and this a decided one—the factor must act on similar cells of isogenic mice of the same strain. Suggestive too is the observation by Little that the tumour, once started, increases in size not so much by actual division of the tumour cells as by transformation by the "milk factor" of cells which have been produced hyperplastically by oestrogenic stimulation, a point of interest also in connexion with the transmission of the condition by the milk to other mice. In such a process a "chain reaction" would appear to take place—the factor producing its specific effect and at the same time reacting with the genotype of the secreting cell to produce more "milk factor."

The "milk factor" would seem therefore to be an aberrant hormone which has made its appearance through the removal of certain dominants and their replacement by harmful recessives in the process of inbreeding. The present discussion, though for the most part an interpretation of recognized facts, has in places taken a mildly speculative turn, to a very much less degree, however, than that undertaken by Dr. Andrewes in his lecture. In any case, the argument thus presented will require to be effectively countered before there can be put in its place the virus theory, based as this is solely on the occurrence of multiplication and transmission of the agent, with complete disregard of the implications of the part played by genic and hormonic factors.—I am, etc.,

Aberdeen. J. P. MCGOWAN.

"Autemphysesis"

SIR,—While serving in the Sudan in the days before the murder of Sir Lee Stack led to the withdrawal of Egyptian troops I came across a number of cases of what Mr. Philip Reading describes as "autemphysesis" (January 14, p. 105), though we had a less polite name for it.

Service in the Sudan was unpopular with the rank and file of the Egyptian army, and various ingenious tricks were tried to obtain invaliding to Egypt, among them being multiple puncture of the buccal mucosa with a large needle used for sewing sandbags which had a triangular cutting blade. Subsequent blowing produced signs identical with those described by Mr. Reading. Epidemics of the complaint tended to coincide with the arrival of a new medical officer but were, needless to say, short-lived—the "treatment" having painful associations with another part of the body.—I am, etc.,

Beccles, Suffolk. C. GRANTHAM-HILL.

Ankylosing Spondylitis Treated by Spinal Osteotomy

SIR,—Having learned the operation of spinal osteotomy from Smith-Petersen, I naturally have a special interest in this operation, and I have a personal series of some 18 cases. The case described by Mr. F. Wilson Stuart and Mr. G. K. Rose (January 21, p. 165) showed a good result, but there are some points with regard to the operation which require stressing.

1. The indications are not merely on cosmetic grounds but to enable the patient to see ahead and to relieve chest and gastro-intestinal disturbances, the result of pressure of the costal margin on to the abdomen.

2. The prone position is a perfectly satisfactory one in which to carry out the operation, and it is almost essential, as when the osteotomy has been completed and the correction is being obtained this must be done with perfect control on a table which allows hyperextension and under direct vision.

3. The complete correction must be obtained in this phase and checked if necessary by radiological control. At the end of this stage the base of the spinous process above should rest on a shelf formed from the remains of the spinous process below the level of the osteotomy in a suitable position, so that no further displacement can occur during the final part of the operation. This consists of closure of the wound in layers and the application of a plaster jacket.

4. It is absolutely essential to rupture the anterior longitudinal ligament in the course of the correction. If this is calcified or ossified it gives way with a loud snap. If it is still fibrous there is a soft thud, but no real correction can be obtained without the anterior longitudinal ligament being ruptured, and in none of my cases has an operation been necessary to achieve this division.

5. It is quite easy to carry out spinal fusion at the same time as the osteotomy, the cancellous bone chips removed from the osteotomy site being extremely valuable in supplementing the ordinary Hibbs's type of fusion. Fusion is readily obtained in these cases of ankylosing spondylitis, and in all my cases fusion has been sound within three months. It has been necessary to keep these patients recumbent for six weeks only, and for the second period of six weeks the patient is up in an ambulatory jacket.

6. Up to date I have had no serious trouble with post-operative complications, but ileus and root irritation and shock from the continued bleeding of the raw bone area must be anticipated.

7. In many cases of ankylosing spondylitis there are also fixed flexion deformities in the hip-joints, and in many of these cases correction of the hip-joint deformity by either arthroplasty or pseudarthrosis, with relief from the flexion deformity, will render spinal osteotomy unnecessary.—I am, etc.,

London, W.1. W. ALEXANDER LAW.

Murder and Insanity

SIR,—The Lord Chief Justice is reported (January 21, p. 196) to have stated before the Royal Commission on Capital Punishment that the jury decided the question of insanity, and that

"it seemed most improbable that Parliament should ever have intended to give two or more medical practitioners power to reverse the findings of a jury by means of a private inquiry, a power given to no other persons or court in the country, and which certainly the Court of Criminal Appeal did not possess."

I hope you will forgive me if I doubt the accuracy of this report, as it seems to me doubtful whether Lord Goddard made, in fact, such a statement without qualifying it considerably. I think there can be few trials in which the question of insanity is raised and in which the judge does not impress on the jury and medical witness that the most important point at issue is that of criminal responsibility as defined in the M'Naghten Rules and not just that of insanity. This, then, is the question which a jury is required to answer—whether the accused was responsible at the time of committing the act, and not whether he suffered from a mental illness. If the jury find that the M'Naghten Rules apply they will return a verdict of "guilty but insane." If they do not do so it does not follow that they have found him sane. It happens quite frequently that the jury find the accused responsible when, according to medical evidence, he is mentally ill. As it goes against the feeling of the community to execute somebody who is ill the Home Secretary recommends a reprieve in some such cases.

It does not seem right to say that two or more medical practitioners have the power to reverse the finding of a jury. The medical practitioners report to the Home Secretary, who has the power to recommend, or not to recommend, a reprieve, having seen this and many other reports relevant to the case. I think it is most undesirable that such steps should be taken as administrative measures, shrouded in secrecy. What I regard as desirable is an alteration of the law to make such frequent administrative measures unnecessary.—I am, etc.,

Wickford, Essex. S. L. LAST.

Antihistamine Drugs for Pleural Effusions

SIR,—Some months ago, encouraged by the widespread use of antihistamine drugs in the treatment of allergic conditions, I decided to investigate the effect of pyranisamine maleate on tuberculous pleural effusions. The work of Petroff and others suggests that these effusions are allergic in nature. Unfortunately I see few cases of acute tuberculous pleural effusions, but up to date I have gained the impression that pyranisamine maleate may prevent the further exudation of fluid in acute effusions, especially those complicating pneumothorax treatment. It has, of course, no influence on the rate of absorption.

In view of the fact that pleural effusions are so variable in their behaviour, a very large number of cases would have to be treated before the efficacy of this treatment could be assessed. I am therefore submitting this letter in the hope that it will stimulate others, who see more of these cases than I do, to give it a trial.—I am, etc.,

Belfast. R. FAWCETT STRONGE.

Diagnosis of Perforated Peptic Ulcer

SIR,—There are few more easily diagnosed acute abdominal conditions than a typical case of a perforated peptic ulcer, but, as Zachary Cope[1] points out, there are many variations of the typical clinical picture. For instance, a previous history of dyspepsia may be lacking, and the patient's description of the severity of the pain varies from case to case—"One man's ache is another man's agony." The patient may not appear to be distressed in any way and may move about the bed without discomfort.

In three of the twenty cases operated on by me in the Edgware General Hospital in the last two years board-like rigidity was limited to the upper abdomen. Below the umbilicus the musculature was almost completely relaxed, although free fluid was present. Palpation does not always aggravate the pain, and in only a few cases can shifting dullness be sufficiently marked in the early stages to leave no room for doubt. Diminished liver dullness is only present in a minority of cases, as is tenderness in the pouch of Douglas.

It is most important, of course, to distinguish a perforated peptic ulcer from other causes of acute abdominal pain for which operation is not only unnecessary but actually contra-indicated. These are (1) biliary or renal colic, (2) gastric crisis of tabes dorsalis, (3) acute pulmonary infections affecting the lower lobes and diaphragmatic pleura, (4) acute exacerbation of peptic ulcers without actual perforation, and (5) abdominal pain of cardiac origin. Typical cases of any of these will usually speak for themselves, but in cases of doubt valuable time may be lost by the over-cautious surgeon in waiting for classical clinical features to appear, and unnecessary explorations may be carried out by the impulsive.

There is one method of examination, however, on which I place much reliance, and that is auscultation of the abdomen. In any of the above-mentioned conditions normal bowel sounds can be heard, but I have yet to see a patient with a perforation in whom bowel sounds were not feeble or absent altogether.—I am, etc.,

Edgware, Middlesex. G. R. C. PEATFIELD.

REFERENCE

1 *The Early Diagnosis of the Acute Abdomen*, London, 1946.

Libel Action by Mr. Matthias Alexander

SIR,—The brief announcement in your columns (December 10, 1949, p. 1359) that Mr. F. M. Alexander has won his action for libel against the South African Government marks the close of a remarkable legal action. The reports, however, which you have given of the case to date do not in our opinion give a completely faithful account of the matter, taken as they were from the columns of a daily newspaper (the *Cape Argus*) and not from the actual court proceedings.

When an action like this has been fought and won, it is certainly best for the unfortunate participants to let the matter drop with as little fuss as possible. Before this happens, however, we would like to stress some of the points which may not be clear.

The action was undertaken only after several months of patient and reasonable requesting by Alexander that the alleged defamation should be withdrawn. The defamatory article appeared in a South African Government publication, and the Government Attorney was briefed to defend the authors in what was to become one of the most important libel actions on record. Funds were forthcoming to enable Dr. E. Jokl, the chief author of the defamatory article, to come to England and to enlist the support of some of the most eminent medical

scientists in this country. In his judgment Mr. Justice Clayden pointed out at some length that since none of them had actually investigated Alexander's work in operation they found themselves in a difficult position.

When you published in your columns that Alexander's work was found to be "not entirely worthless" and left it at that, was not this perhaps an understatement? What Mr. Justice Clayden said in his actual judgment was:

"The defendants have in my view failed to establish that the system is unsound. They have shown that Mr. Alexander supports his technique by wrong physiological reasoning, and by reference to work which almost certainly has nothing to do with it. But that in my view is not enough. In regard to the claims to prevent diseases, the defendants in the article said that a claim was made to prevent practically every known disease. This was not, I think, claimed in Mr. Alexander's books. In regard to the diseases which he does claim to prevent, though I am far from saying that the evidence shows that claim to be sound, yet I consider that the defendants have not proved the negative they had to prove: they have not shown that what might lead to improved health might not prevent diseases for which either the causes, or factors which build up resistance, are not fully known. They have failed in my view to prove that the system cannot bring about the results which it does claim in the improvement of health and the prevention of disease, and again they have made matters worse by overstating the claims made for the system. The claim to improve health has not been shown to be baseless, even in the medical field."

The evidence eventually ran to over 450,000 words, and the case has taken five years to complete. Alexander has now been granted damages and all costs, which were extremely large. In view of the gravity of the financial risk, the action was a courageous gesture from a private individual against a highly organized and wealthy opposition, and could have been taken only by a man confident of the value of his work and of its ability to stand up to the strongest barrage of scientific authority that could be found.

A suggestion was made some twenty years ago that doctors should train in this method and investigate it (*British Medical Journal*, 1926, **2**, 1221). Just before the war nineteen doctors signed an appeal which appeared in your columns suggesting that the time was ripe for a full investigation (1937, **1**, 1137). Writers to your and other medical journals have stressed the importance of Alexander's work. We should like to close with a plea, as two of the doctors who have made a detailed personal study of the method and who have incurred some unpopularity by supporting Alexander. Research is made into methods of prevention and treatment which have much less proved value than the Alexander method can claim. There is an obvious need now for a suitably sponsored investigation to determine the full scope and applicability of the method into medical problems of prevention and rehabilitation, for it may well make some of the present expenditure in the curative sphere ultimately unnecessary.—We are, etc.,

WILFRED BARLOW.
DOROTHY MORRISON.

London, S.W.7.

Birth Weight and Subsequent Weight

SIR,—I was interested to read Professor R. S. Illingworth's article on birth weight and subsequent weight (January 14, p. 96). I should like to inquire whether there is any record of the proportion of these babies who were breast-fed, and also whether the artificially fed babies had their feeds calculated on birth weight, as is the current paediatric practice. I feel this method is designed to perpetuate thinness in the thin and fatness in the fat.

The premature babies in the series were probably privileged to receive for a time 60 calories per lb. (454 g.) as against 50 calories per lb. for the heavier babies, but it is doubtful whether this concession is adequate in all cases. It appears illogical that a thin baby weighing, say, 6 lb. (2.7 kg.) should be estimated to require 300 calories daily, whereas one with a good layer of subcutaneous fat weighing 8 lb. (3.6 kg.) is estimated to require 400 calories daily. Again, if the former baby proceeds to lay down subcutaneous fat and thereby increases his weight by a half-pound or more weekly for a few weeks there is a tendency to consider this an excessive weight gain—in my opinion mistakenly.

I feel that this present system does not allow sufficiently for individual variations, and I would urge that more latitude should be allowed to the mother when giving advice on feeding. She is the one person who will invariably treat her baby as an individual and strive to achieve optimum results with an individual baby. One most successful mother remarked to me that she always made up feeds in accordance with the doctor's advice, but if the baby was hungry she heaped her measures, whereas if he was not hungry she levelled them off. This seemed very satisfactory in practice.

It should be quite possible to suggest approximate feeds, taking into account both weight and state of nutrition, and to encourage the mother to give more or less as she finds necessary. Provided the infant is healthy, the feed suitable and properly given, and the wind is brought up well during and after feeds, an infant's appetite is a good guide to its needs, and the mother will soon learn to adjust feeds as necessary. Further supervision and advice should be given in such a way as to increase rather than diminish the mother's self-confidence.

Many a young mother feels her first real sense of responsibility when she sees her baby so utterly dependent on her, and it is important for the welfare of the family that this should be fostered. If the mother is made to feel that she is incapable of managing her infant's feeds, and if all details are worked out by mathematical formulae incomprehensible to her, she will naturally tend to rely more and more on outside help, to the great detriment of the family.—I am, etc.,

London, W.C.1. JOAN TANNER.

Group and Individual Methods of Treatment

SIR,—Drs. A. S. Thorley and N. Craske (January 14, p. 97) compare the results of group and individual methods of treatment. Group therapy was used by Dr. Thorley and an individual approach by Dr. Craske. In their elaborate and painstaking analysis of results they appear to overlook an important point—the personality of the physician controlling treatment. This I believe to be a most significant factor in assessing the results of any form of psychiatric treatment.—I am, etc.,

Dublin. FRANK MCLAUGHLIN.

Three-quarters of a Fatality

SIR,—I note from Professor Geoffrey Jefferson's paper "Surgery, 1900–1950" (January 7, p. 8) that in the last 50 cases in which Mayo Robson removed gall-stones from the common bile duct prior to his publishing his results in 1903 he achieved a mortality of 1.5%. Am I to conclude that the unfortunate deceased was only "nine to the dozen"?—I am, etc.,

Christleton, Chester. ARNOLD BROWN.

*** The relevant passage in Mayo Robson's paper (*British Medical Journal*, 1903, **2**, 240) is as follows: "Whereas in my first series before 1900 the rate of mortality was 23.8%, in my last series it is only 1.5%, and I have had a continuous series of 50 cases without a death."—ED., *B.M.J.*

History of Westminster Hospital

SIR,—The Board of Governors of Westminster Hospital have commissioned Mr. John Langdon-Davies to write the history of the hospital since its foundation in 1719. It is intended that apart from recording the hospital's activities the book shall be a social history of the conditions which brought the voluntary hospital movement into being at the beginning of the eighteenth century, and which led to the founding of our hospital.

We should be grateful for the assistance of anyone who possesses documentary or other material useful for the writing of the history, and particularly for any reminiscences or notes about the hospital which past or present members of its medical staff would care to contribute. All original material will be carefully copied and returned. Information or inquiries about the history should be addressed to me.—I am, etc.,

CHARLES M. POWER,
House Governor and Secretary.

The Westminster Hospital,
London, S.W.1.

POINTS FROM LETTERS

Failed Forceps

Dr. E. PROTHEROE SMITH (Crediton, Devon) writes: When practising in an industrial town where many young married women sat at work, I found that occipito-posterior positions were the commonest cause of prolonged labour. *Propter hoc?* I found these two methods useful in the second stage and, on the whole, easy. First, with "short straight" forceps gripped firmly in the hand, rotate the head a little at a time between pains, lifting the head slightly in the pelvis and relaxing the blades during a pain, till the occiput is behind the pubis. A thread tied on one handle prevents any doubt about this and avoids further examination. The head in most cases can now be delivered easily, without altering the forceps. Secondly, the same method can be used with ordinary forceps, but the handles must be carried through a large arc to keep the blades in the axis of the pelvis. If slight traction does not now bring the occiput to the perineum the forceps must be reapplied, keeping two fingers on the side of the head to prevent it twisting back. I never saw any trauma resulting from this manœuvre, which I believe was used many years ago but fell into disrepute.

With Whales and Seals

Dr. F. R. C. CASSON (London, W.1) writes: Could Dr. H. R. Lillie inform those of us who, like Dr. E. T. Everdell (January 14, p. 128), feel that something should be done to stop the appalling cruelties described in his article (December 24, 1949, p. 1467) what practical measures we may take? It is not enough to shudder and turn over the page.

Treatment of Herpes Zoster

Dr. T. C. HALLINAN (Frome, Jamaica, B.W.I.) writes: The treatment of herpes zoster has always seemed to me to be very unsatisfactory, but about eight years ago, while serving with the R.A.M.C., I fortuitously chanced upon a form of treatment which has given excellent results in all cases I have treated since, and as I have not heard of anyone else using it I venture to submit the details in case the treatment may be of help to others. It consists of applying either tannic acid jelly, gentian violet jelly, or triple dye jelly to the lesions, allowing the jelly to dry, and covering with lint or gauze (mainly to avoid staining of clothing). The application is repeated if any of the blisters burst. The relief afforded is quick, and the condition usually clears up in a few days; neuritic after-pains are very rare. If irradiation with infra-red rays on three or four occasions is possible as well, this speeds up the cure considerably. I have used this form of treatment on about 300 cases and have obtained uniformly good results and no failures.

The Lights Go Up

Mr. F. H. BADCOCK (Bury St. Edmunds, Suffolk) writes: In connexion with the reports of shot in the appendix by Dr. C. Eppel (December 24, 1949, p. 1454) and Dr. J. A. G. F. Rose (January 21, p. 191), I was told many years ago of an old lady who, on an inquiry for her health, replied somewhat like this, "I be a bit troubled with the risin' of me lights, but I takes some shot now and then, and that keeps 'em down." "Rising of the lights" was formerly a recognized complaint. Was shot a recognized remedy?

A Case of Human Myiasis

Dr. G. E. FFRENCH (Halifax, Nova Scotia) writes: The interesting case reported by Dr. Hellmutt W. F. Brauneck (December 10, 1949, p. 1335) reminds me of the reference to the recognition of vermin-infested ears (krimi-karna) in the *Samhita* of Sushruta, which forms the basis of present knowledge of Ayuvedic medicine, still practised throughout the countries of India and Ceylon. It is of interest to recall that Sushruta lived about six hundred years before Our Lord: his works have been translated into English (Bhishagratna, 1916, Calcutta).

The Training of General Practitioners

Dr. P. G. HILL (Bristol) writes: As I was one of the trainee-assistants mentioned by Dr. F. Charlotte Naish (January 21, p. 192) I would like to correct an impression which might have been made by her last paragraph. While a student I was frequently taught how to pass a catheter, but never that to do so in a labouring woman was easy. I would like to add that I feel my period of training under Dr. Naish, most conscientiously carried out by her, has been of great help to me in trying to understand the many problems which at some time must also have caused anxiety to others attempting general practice for the first time and desirous of keeping up as good a standard as possible.

Obituary

Dr. THOMAS GLYNN MORRIS died at his home in West Derby, Liverpool, on January 1 at the age of 80.

One of the best-known general practitioners in Liverpool, he was educated there at the Collegiate School and University College, took his L.S.A. in 1895, and graduated M.B., Ch.B. in 1896. He first practised in Nantlle, Caernarvonshire, and, as medical officer to the extensive slate quarries there, he acquired particular skill in dealing with accidents and fractures. Returning to Liverpool at the beginning of the century, he joined his uncle, the late Dr. Hugh Williams, in Everton, and continued in practice there until a stroke, on the fiftieth anniversary of his qualification, forced him to retire in 1945. He was always interested in ophthalmology, and during the 1914–18 war he acted as clinical assistant to the eye department of the Royal Infirmary. He wrote a thesis on ophthalmia neonatorum which gained him his M.D. in 1918, and he was for many years an examiner for the National Association of Opticians. At the end of the war Dr. Morris took into partnership the late Dr. C. G. Skinner, and himself moved to West Derby, where he rapidly extended his practice. On the death of Dr. Skinner in 1931 he was joined in practice by his son, Dr. Mansel Glynn-Morris. An exceptionally active man, both mentally and physically, he spent all his leisure acquiring further knowledge and extending his general interests. He became an expert on pictures and books, and built up good collections of both, being especially interested in the Old Water Colour Society and in Welsh literature. He was a member of several archaeological and antiquarian societies, and a keen geologist; he was elected a Fellow of the Geological Society, and became president of the Liverpool Geological Society. Dr. Morris was also an enthusiastic pioneer motorist, and in 1897 was the second man to take a car into Anglesey; he was one of the original members of the Automobile Association. A keen Methodist, he was for many years a deacon at Fitzclarence Street Chapel.

He joined the B.M.A. soon after qualifying, and in 1935 he travelled to Australia to the B.M.A. meeting there; he was also a prominent member of the Liverpool Medical Institution. A good clinician and a conscientious physician and obstetrician, he was a true family doctor, a kindly friend and counsellor to all his patients in every walk of life. His death has brought sorrow to all who had known and loved him.—M. G.-M.

Dr. ROBERT ERIC HENRY, of Baker Street, London, N.W.1, died suddenly on January 11 at the age of 51. "Eric," as he was known to a wide circle of friends in London and Australia, is mourned by all who knew him and admired his cheery smile, generous nature, and courage in adversity. He was born in the Nepean district of New South Wales just inland from Sydney, and was educated at the Sydney High School and at Sydney University, where he began the study of medicine in 1915. After completing the first year, he enlisted and served with the A.N.Z.A.C.s for three years, chiefly in France, where he was wounded in the knee. In 1919 he returned to his interrupted medical studies, and graduated M.B., Ch.M. in 1923. The next three years were spent in resident appointments at the Royal Prince Alfred Hospital and the Western Suburbs Hospital, Sydney, and at Toowoomba Hospital, Queensland (1923–6). Dr. Henry then gained further experience in general practice before travelling to England in 1930 for postgraduate study in London with a view to specializing in ophthalmology. In 1931–2 he was house-surgeon at the Royal Eye Hospital, London, and he obtained the D.O.M.S. in 1932. Shortly afterwards there was an epidemic of poliomyelitis in South London, and unfortunately in September, 1932, Dr. Henry was one of those affected. After almost a year of treatment in the Metropolitan Hospital and two more years at the Dame Agnes Hunt Orthopaedic Hospital, Oswestry, he returned to London in 1935, undaunted and with his familiar smile, although barely able to stand erect and walk even a limited distance with leg callipers and his "two sticks." He consistently rejected any kind of help or social commiseration, and in 1936 he started

practice again as an ophthalmic specialist. Although precluded from surgery, which necessitates standing, he served faithfully and well the three eye hospitals of his choice. At the Royal Eye Hospital he was a first assistant. At the Central London Ophthalmic Hospital he was lecturer in the Orthoptic Department, a post which he continued to hold when this hospital merged with Moorfields Eye Hospital, where also he was a chief clinical assistant. During the war period he remained throughout in his Baker Street flat, which became a haven of refuge for his many Service friends. Also, he extended his activities and worked harder than ever, ignoring and suffering without complaint London's wartime discomforts and dangers.

Eric was a characteristic and unrepentant Australian of the most generous and lovable kind. The strain of working daily to the limit of his physical endurance undoubtedly contributed to his dangerous rise of blood pressure, which he was aware of but would never discuss. He had not seen his homeland since leaving it in 1930, and whatever his reasons, premonitory or otherwise, he decided to make a brief visit in 1949. He flew to Sydney in September, and enjoyed meeting many Australian relatives and old friends. In October he made the return flight to London. For two months after his return he was ill and confined to his flat, unable to work. By Christmas he insisted that he was better, but it was perturbing for his friends to observe the loss of strength and the change in his appearance. Nevertheless, with his habitual steadfast courage, he returned to work, but for a few days only, and then a cerebral haemorrhage sadly ended what may truly be described as a wonderful example of fortitude and determination to be independent and to succeed in practice under the difficult restrictions imposed by two paralysed legs and, latterly, a high blood pressure. Eric Henry will be grievously missed, but his cheerful courage and determination will long be remembered.—H. H. S.

Medico-Legal

FATAL HEPATITIS DUE TO IRON POISONING

In Glasgow on January 19 a fatal-accident inquiry[1] was held into the death of Marcella Mary Byrne, or Restrick, aged 26. Her husband said that his wife was the mother of two perfectly normal children. However, when she had her last child she had been delivered in hospital because her blood was Rh-negative and it was feared that the baby might suffer from some congenital defect. His wife was particularly concerned about the possibility that she might have a "blue baby." Last year she thought that she was pregnant again, and on October 22, on the advice of a woman she had met on a bus, she had taken a mixture of iron and ammonium citrate and whisky, and she had been sick. She became ill the next day, and on October 24 she was admitted to the Victoria Infirmary, where she died the following day.

A dispensing chemist said that he had provided the woman with sixpennyworth of iron and ammonium citrate—about ½ oz. (15 g.). He said it was an unusual purchase but not altogether uncommon. Ferri et ammon. cit. was used extensively in making up tonics and prescriptions and did not come under the Dangerous Drugs Act.

Dr. J. A. Imrie, who is chief medical officer of the Glasgow police, said that iron taken in large quantities could prove fatal. He had not been able to find a record of any similar case in an adult, but iron preparations had caused death in young children.

Sheriff-substitute Johnston said that it was a chance in a million that any particular person should be affected in that way by what seemed to be a familiar type of drug. It would seem, however, that some foolish woman had informed the other woman, quite mistakenly, that if she took the drug it would be likely to cause abortion.

The jury then returned a formal verdict that the woman consumed ½ oz. of iron and ammonium citrate and that her death was caused by the resultant toxic hepatitis.

An annotation on the subject of iron poisoning appears elsewhere in this issue (p. 293).

[1] *Glasgow Herald*, January 20, 1950.

Universities and Colleges

UNIVERSITY OF WALES

The following candidates for the degrees of M.B., B.Ch. at the Welsh National School of Medicine have satisfied the examiners at the examination indicated:

HYGIENE.—L. M. Charles, D. W. Evans, S. E. Ll. Morris, S. J. S Polwin, Elizabeth M. M. Price, J. W. Rees, T. B. N. Richards, D. B Scourfield, Esther H. Thomas, D. S. Wood.

OBSTETRICS AND GYNAECOLOGY.—D. F. Brown, Josephine J. Candy, L. M. Charles, D. E. Copas, B. M. Davies, S. I. Davies, J. M. S Dixon, J. L. A. Dowse, D. R. T. Evans, D. W. Evans, J. Evans, B. J. Fudge, S. G. Gang, T. Griffiths, Nansi G. Gwynne, A. J. Hooper, J. Magell, W. B. Morgan, *E. D. Morris, S. E. Ll. Morris, T. L. Morris, G. J. Moses, D. Phillips-Miles, Elizabeth M. M. Price, Margaret Pugh, D. Rees, D. St. J. D. Rees, T. A. I. Rees, D. B Scourfield, A. P. Thomas, Margaret E. Thomas, Margaret H. J Thomas, *Ann G. Tighe, D. S. Wood.

*With distinction.

UNIVERSITY OF BIRMINGHAM

The following medical degrees were conferred on December 16:

CH.M.—J. N. Wilson.

M.B., CH.B.—Joyce Bott, D. W. Davis, D. A. Gale, P. L. Goode, C. C. Griffiths, K. A. G. Guy, R. S. T. Hey, Pauline M. Higgins, I. E. J. McLauchlan, B. MacMahon, E. T. Mathews, Mary S Medcalf, Jeanne C. Poppitt, L. E. Tyler, Ruth A. Watson, P. S. W. Wilkins, E. W. Witherspoon.

ROYAL COLLEGE OF PHYSICIANS OF LONDON

At a meeting of the Royal College of Physicians of London held on January 26, with the President, Lord Moran, in the chair, the following representatives of the College were elected: Dr. W. G. Wyllie, on the Council of the National Association for Mental Health; Dr. W. E. Hume, on the Council of King's College, University of Durham; Dr. Cyril Elgood, at the installation of Princess Alice, Countess of Athlone, as Chancellor of the University College of the West Indies; Sir Weldon Dalrymple-Champneys, at the Health Congress of the Royal Sanitary Institute to be held at Eastbourne from April 24 to 28; Dr. Donald Hunter and Dr. Philip Hamill, to represent the College on the newly constituted Joint Formulary Committee; and Dr. A. S. Barnes, on the Court of Governors of the University of Birmingham.

Membership

The following candidates having satisfied the Censors' Board were elected Members of the College:

Unity R. Allen, B.M., H. J. G. Bloom M.D., F. G. Bolton, M.B., J. P. Bound, M.D., C. D. Calnan, M.B., J. N. C. Cooke, M.B., L. G. G. Davies, M.B., J. J. Y. Dawson, M.D., G. C. de Gruchy, M.D., N. A. Durham, M.D., C. J. Earl, M.B., Flying Officer, R.A.F., A. W. B. Edmunds, M.B., J. W. L. Edwards, M.B., J. J. Fleminger, M.B., D. K. Ford, M.B., H.-J. B. Galbraith, M.B., D. B. Gash, M.B., P. A. I. Gorer, L.R.C.P., W. P. Gurassa, M.B., R. C. Hallam, M.B., P. C. Harris, M.B., R. Hierons, M.B., C. G. Hunter, M.B., Surgeon-Commander, R.N., Joan B. T. Logan, M.D., K. W. Lovel, B.M., G. R. W. N. Luntz, L.R.C.P., B. E. W. Mace, M.B., I. R. Mackay, M.B., N. B. Malleson, M.B., A. Meiklejohn, M.D., J. P. Mostyn, M.B., T. E. Parry, M.B., Velva Schrire, M.B., R. Seidelin, B.M., S. J. Steel, M.D., J. K. Steward, M.B., F. H. Stone, M.B., A. I. Suchett-Kaye, M.D., J. H. Thomas, L.R.C.P., D. C. Turk, B.M., E. G. Walsh, M.D., J. N. Walton, M.B., J. K. G. Webb, B.M., Ann H. Willcocks, M.B., J. M. Winn, L.R.C.P., F. J. Y. Wood, M.B., A. Wynn, M.D.

Licences

Licences to practise were conferred upon the following 135 successful candidates (including 27 women) who have passed the final examination in Medicine, Surgery, and Midwifery of the Conjoint Board and who have complied with the by-laws of the College:

R. J.-D. Abraham, E. Ap-Cynan, H. G. Arnall, G. Ascough, E. A. Badoe, A. M. Baker, D. Barker, J. L. R. Barlow, R. Barnes, L. M. Barrett, P. S. I. Barry, Mary Bateman, J. D. Beavan B. B. Beeson, C. A. Bentley, W. K. E. Bernfeld, N. P. Bhandari, Helen M. Bishop, Irene F. A. Blakeney, S. D. Bradley, B. I. Brest, J. W. E. Bridger, W. A. Bullen, R. G. Bunn, P. Burrows, S. A. Busk, F. G. T. Carter, N. F. Cockett, R. F. Coggins, June P. Cooper, H. M. C. Corfield, L. Crystal, Margaret C. D. Daniel, Edith Danos, Eluned B. Davies, D. S. Davis, Sheila F. Dawson, Vivienne d'Andria, Kathleen M. de Ville, J. C. Doran, J. B. Dossetor, D. W. A. Drew, W. E. Earle, I. D. Edeleanu, P. C. Farrant,

G. A. Faux, D. L. Fox, C. J. Frederick, D. A. Gale, A. Gardner, S. R. Ghosh, W. S. Goodman, E. J. Goodsir-Cullen, R. E. G. Gosling, R. Goulding, J. P. Green, Jean E. Griswood, Jean M. Halliwell, P. J. Hammett, C. G. J. Hardy, Ruth F. Harris, Helena J. Harthoorn, B. Hartley, H. R. Hewitt, Frances M. Hill, Barbara D. Holton, Pamela J. Houchin, S. Hulme, G. H. Isaac, S. M. H. Jaffari, F. T. Jenkinson, E. Ll. Jones, G. Kennedy, M. Koziol, E. B. Kraus, S. T. Langham, J. H. Latham, J. F. Le Clus, J. P. Lester, J. C. Lindsay, D. H. Lloyd, J. MacDermot, I. F. G. McLannahan, M. Mason, K. R. Mason-Walshaw, G. A. Medhurst, H. A. Mitchell, H. D. S. Morgan, R. Ll. Morgan, V. C. Morris, Cicely M. Murphy, B. E. C. Nordin, Margot L. S. Norton, Aideen E. T. O'Brien, J. B. Parton, C. J. Pereira, J. M. Pirrie, W. A. Pollitt, J. A. Porritt, N. A. Power, F. R. M. M. Prat, Lucy J. Putnam, A. E. A. Read, J. D. Rees, D. W. Robertson, B. R. Robinson, K. F. Robinson, W. Rodger, J. J. O'C. Rorke, I. Rosen, J. E. Routh, Stella Salt, Noel P. Shannon, Mary Soppitt, P. B. Sparke, J. T. B. Stewart, G. P. Tannen, E. A. Tarleton, Susanne M. Tauber, J. D. Thomas, P. D. S. Thomas, D. C. Thompson, L. E. Tyler, W. N. Vellacott, Claudine M. R. Vesey, F. P. Wallis, Cecilia M. Ward, W. H. Watson, W. W. Watson, R. H. R. White, P. L. G. Williams, P. F. Willis, D. A. Wright, H. Yellowlees, N. W. H. Young.

Diplomas

Diplomas in Anaesthetics and in Public Health were conferred jointly with the Royal College of Surgeons of England to the following successful candidates:

DIPLOMA IN ANAESTHETICS.—H. M. A. Ansari, A. W. H. Ashbery, W. L. M. Bigby, P. J. C. Burton, Elizabeth P. Champion, K. A. Cowan, H. T. Davenport, W. F. O'M. Doherty, A. W. Edridge, A. Farr, S. A. Fleming, N. H. Georgeff, W. R. Gilmore, E. Goldsmith, I. M. Gow, W. A. Groom, G. F. Hawkins, F. W. Hill, H. Howell-Jones, J. W. Keighley, Marie D. Kelleher, L. G. Kilpatrick, C. R. Kirkpatrick, J. R. Kyles, W. E. Lawes, J. W. Lewis, T. McErvel, Eileen M. MacMahon, J. Q. Matthias, J. W. Monro, Kathleen M. F. Murray, S. L. Nath, J. G. Pegg, J. F. Pelmore, C. F. G. Prideaux, W. E. Quitman, G. H. Rea, A. L. Reynard, J. D. Scobie, D. A. Sherman, J. H. W. Smith, S. D. K. Stride, J. W. Thomas, N. C. B. Trapps, Simone J. Van Son, T. E. Waine, J. T. Wheldon, J. D. Whitby, H. O. White, W. R. D. Wiggins.

DIPLOMA IN PUBLIC HEALTH.—J. C. Day, R. Franey, W. C. Kingston, D. D. Maitland, J. McG. Rogan, A. Singh, W. M. Stewart, P. Westcombe.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—F. O'D. Finigan, and to the seven successful candidates whose names were printed in the report of the meeting of the Royal College of Surgeons of England in the *Journal* of January 28 (p. 257).

Diplomas in Tropical Medicine and Hygiene, in Laryngology and Otology, in Medical Radiodiagnosis, in Medical Radiotherapy, and in Industrial Health were conferred jointly with the Royal College of Surgeons of England to the successful candidates whose names were printed in the report of the meeting of the Royal College of Surgeons of England in the *Journal* of January 28 (p. 257).

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

Dr. G. J. Aitken will deliver the James Watson Prize Lecture in the Hall of the Faculty (242, St. Vincent Street, Glasgow) on Wednesday, February 8, at 5 p.m. His subject is "Recent Advances in the Diagnosis of Congenital Heart Disease." Medical practitioners are invited to attend the lecture.

At a meeting of the Faculty held on January 9, with the President, Dr. W. R. Snodgrass, in the chair, R. A. Patel was admitted a Fellow of Faculty *qua* Surgeon.

SOCIETY OF APOTHECARIES OF LONDON

Dr. J. P. Hedley has been re-elected as the Society's Representative on the General Medical Council.

The Diploma of M.M.S.A. was granted to A. C. Sinha, upon examination.

The Diploma of L.M.S.S.A. was granted, upon examination, to the following successful candidates: S. S. Maré, A. K. Doust, E. T. King, J. S. G. P. Stableford, T. M. Morgan, S. A. Jolliffe, C. W. Shaw, A. R. Davis, C. D. Bulstrode, J. A. Payne, J. A. Bloomfield, B. R. J. Simpson, M. Benjamin, G. P. Sugden, W. B. Cook.

FACULTY OF RADIOLOGISTS

The following candidates satisfied the Board at the 1949 examination for the Fellowship of the Faculty: *Radiodiagnosis:* J. Dawson, M.D., W. D. Nichol, M.B., Ch.B., O. E. Smith, M.B., Ch.B., R. E. Steiner, M.B., B.Ch., A. A. Vickers, M.B., B.S. *Radiotherapy:* E. C. Easson, M.B., Ch.B., M. G. El D. Massoud, M.B., B.Ch., W. Shanks, M.B., B.Ch.

Medical News

Award for Vascular Surgery

Dr. Alfred Blalock has received the Rudolph Matas award for his work in advancing vascular surgery. It was presented by Dr. Matas at Tulane University after a lecture by Dr. Blalock on the surgery of cardiac abnormalities. Dr. Blalock is director of the department of surgery at Johns Hopkins University Medical School. The award is made from the Violet Hart Fund, which was established in 1934 by the family of Miss Hart, a New Orleans musician, to honour Dr. Matas. It consists of a gold medal and a bronze replica, together with a miniature watch-chain medal.

Harveian Society of London

The annual general meeting of the Harveian Society of London was held at 11, Chandos Street, W.1, on January 18. A presentation was made to Sir Cecil Wakeley, P.R.C.S., on his retirement from the office of honorary treasurer to the Society. The president, Dr. Desmond MacManus, then gave his address on "Some Reflections on General Medical Practice in the Last Thirty Years." The officers for 1950 were elected, Dr. R. R. Trail being inducted as the new president.

National Institute for Medical Research

The move of the National Institute for Medical Research, from Hampstead to Mill Hill, has now been completed. The Institute is now at: The Ridgeway, Mill Hill, London, N.W.7 (Telephone: Mill Hill 3666). The building at Hampstead previously occupied by the Institute has been retained by the Medical Research Council to house one division of the Institute and the whole or parts of several research units. The address will be: Medical Research Council Laboratories, Holly Hill, Hampstead, London, N.W.3 (Telephone: Hampstead 2232).

Visiting New Zealand and Canada

Sir Henry Dale, O.M., F.R.S., left the United Kingdom by sea on January 26 for a three-months lecture tour of New Zealand and Canada for the British Council. He will lecture mainly to medical and scientific audiences, but a number of public lectures have also been arranged. He is due to arrive in New Zealand on February 26, and after touring the principal towns and universities there he will fly to Vancouver on April 25. His tour of Canada during the ensuing three weeks will include Banff, Calgary, Edmonton, Saskatoon, Winnipeg, Toronto, London, Ottawa, and Montreal. The subjects he will lecture on include the chemical transmission of the effects of nerve impulses, histamine and the antihistamines, the proper place of science in education, and medical research as an aim in life.

Hundredth Anniversary

With the first 1950 number the *Wiener Medizinische Wochenschrift* celebrates its hundredth anniversary. Probably the most interesting feature of this jubilee number is the chronicle in diary form of its history year by year from 1851. But for the immense energy of its first editor, Dr. Leopold Wittelshöfer, the journal would never have seen the light of day. In 1851 no new publication could be started in Vienna without the permission of the all-powerful Governor, Baron Welden. Permission would never have been obtained but for the cunning of Wittelshöfer, who, at an audience with the baron, remembered that the latter had published some articles on botany, and suggested that he should contribute to the new journal. Wittelshöfer's personality made many enemies, and for years many of the professors in Vienna were actively hostile to his journal. The feud ended when the editor was more or less compulsorily retired in 1888. With his retirement the journal lost its enemies but, for a time, its freshness also. The *Anschluss* and the 1939–45 war brought fresh difficulties, and for over a year the journal was, like so many other German medical weeklies, fused into one monthly publication. From this blow it has rapidly recovered.

Chairman of Dental Board

The Privy Council has reappointed Dr. E. W. Fish as chairman of the Dental Board of the United Kingdom for the term ending on July 28, 1954.

Streptomycin Freed in Ireland

Streptomycin for the treatment of tuberculosis has been freed from control in the Republic of Ireland. The Minister for Health there, Dr. Browne, expressed the opinion that control was still desirable, but he felt it would now be ineffective because the Irish Medical Association had opposed control and the Medical Research Council of Ireland had decided to discontinue exercising the control (*Irish Times*, January 19).

Dental Mission for New Zealand

The Ministry of Health states that an official mission is going to New Zealand at the beginning of February to obtain a report on the New Zealand system of school dental nurses. The members of the mission are Professor R. V. Bradlaw, Dean of the Dental School and Professor of Dental Surgery at Durham University; Dr. T. H. J. Douglas, Senior Dental Officer of the Department of Health for Scotland; Dr. H. T. Roper-Hall, general dental practitioner; Mr. W. G. Senior, Ph.D., Principal Dental Officer, Ministry of Health; Dr. A. T. Wynne, Medical Officer, Ministry of Education.

Leprosy Specialists

Dr. Lauro de Souza Lima and Dr. Antonio Carlos Mauri have come from San Paulo, Brazil, on a visit to Britain. Dr. de Souza Lima is chairman of the Therapeutic Controls Committee of the International Leprosy Association.

Argentine Scholarships

Up to twenty scholarships are being offered annually to professional persons wishing to undertake, in Argentina, advanced study related to public health. The scholarships are tenable for one year, or longer if the work carried out merits an extension. An award consists of the payment of passage and a monthly allowance of 1,000 Argentine pesos. The candidate must apply through a public health authority or university in his own country which will undertake to offer him an appointment on his return, which he will take. Further particulars may be obtained from the British Council, 3, Hanover Street, London, W.1, or from the Secretary of the B.M.A.

Manchester Royal Infirmary Old Residents' Club

All members of the Manchester Royal Infirmary Old Residents' Club have now been supplied with details of the dinner to be held at Belle Vue, Manchester, on March 25. Anyone who has held a resident post at the infirmary and has not been notified of this reunion is asked to communicate with the honorary secretary, M.R.I. Old Residents' Club, Manchester Royal Infirmary.

Epsom College Pensions

Applications are invited for two vacant pensions from the Epsom College Margaret and Josephine Hurd-Wood Gift Fund. Every candidate must be (*a*) a registered medical woman, or (*b*) a wife or daughter of a registered medical man, or (*c*) the daughter of a registered medical practitioner. There is no limitation of age. Forms of application are available from the Secretary's Office, Epsom College, Surrey.

Visits to North America

It is hoped that any medical men and women who intend to visit North America will inform the Secretary of the B.M.A. so that information of such visits may be forwarded to the Canadian Medical Association, which is anxious to be of help to doctors from the United Kingdom visiting North America.

Wills

Dr. Basil Nelson Tebbs, of Haywards Heath, left £23,623. Dr. Eric George Battiscombe, of Exmouth, Devon, left £42,966; Dr. John Columba Byrne, of Sheffield, £17,250; and Dr. Michael Edward Cussen, of Ballybunion, Co. Kerry, £3,255. Mr. Robert Milne, of the London Hospital, left £28,561.

COMING EVENTS

Medical Photography

An exhibition of medical photography will be held at the Photographic Department, St. Mary's Hospital Medical School, on February 7–13 (open from 2 p.m. to 6 p.m.; Saturdays, 10 a.m. to 1 p.m.).

Pavlov Centenary

Professor J. Z. Young, F.R.S., will deliver a lecture to commemorate the centenary of the birth of Pavlov in the Physiological Laboratory, University of Cambridge, on Wednesday, February 8, at 5 p.m. His subject is "The Nature of the Learning Process." The lecture is open without fee to all members of the university.

Chadwick Lectures

The following Chadwick Public Lectures have been arranged: February 14, 2.30 p.m., at Royal Society of Tropical Medicine and Hygiene, 26, Portland Place, London, W., Dr. C. Banning (Chief Medical Officer of Public Health, the Hague), "Co-ordination between the Public Health Service and Private Enterprise in Holland: Its Results"; March 14, 2.30 p.m., at Westminster Medical School, 17, Horseferry Road, London, S.W., Dr. C. A. Boucher (Ministry of Health), "The Maintenance of Health by the Prevention of Accidents in the Home"; April 4, 2.30 p.m., at London Missionary Society, 42, Broadway, Westminster, S.W., Mr. C. E. Scholefield, "Rivers Pollution and the River Boards Act, 1948"; June 20, 2.30 p.m., at Royal Sanitary Institute, 90, Buckingham Palace Road, London, S.W., Professor G. M. Fair (Harvard University), "The Engineer in Public Health." Admission to the above lectures is free, without ticket.

St. Thomas's Hospital Musical Society

This society will perform Mozart's "Requiem" on Tuesday, February 14, at 8.15 p.m. (the performance ending at about 9.30 p.m.), in St. Mary's Church, Bryanston Square, London, W.1. The conductor is Mr. W. D. Bower and the organist Mr. J. D. Bower, organist at St. Paul's Cathedral. No tickets are needed.

Medical Film Makers

Four discussions for makers of medical films have been arranged by the Medical Committee of the Scientific Film Association to take place at Guy's Hospital on the third Wednesday of February, March, April, and May from 6 p.m. to 8 p.m. Admission is by ticket only, obtainable on application to the S.F.A., 4, Great Russell Street, London, W.C.1.

Medical Mycology

The Institute of Dermatology is arranging a series of lecture-demonstrations (including practical work) on medical mycology, to be held at the London School of Hygiene and Tropical Medicine during March. Sessions will be held each Monday and Friday afternoon during the month and will start at 2 p.m. Full details can be obtained from the Secretary of the Institute of Dermatology, 5, Lisle Street, Leicester Square, London, W.C.2.

Scientific Methods

The Medical Research Council will hold a conference on "The Application of Scientific Methods to Industry and Service Problems" at the London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, on March 29–31. The following programme has been arranged: *March 29.*—"Scientific Method in Field Surveys": Professor A. Bradford Hill and associated workers (morning); Professor J. R. Squire and Dr. Alice Stewart (afternoon). *March 30.*—"The Improvement of Human Performance by Laboratory Studies": Sir Frederic Bartlett, F.R.S. (morning); Professor W. E. Le Gros Clark, F.R.S., and Dr. T. Bedford (afternoon). *March 31.*—"The Investigation of Health Hazards—Some Recent Work by Medical Research Council Units": Dr. Donald Hunter and Dr. J. M. Barnes (morning); Dr. C. M. Fletcher (afternoon). Applications should be sent as soon as possible and in any case

before March 1 to the Secretary, Medical Research Council, 38, Old Queen Street, London, S.W.1. There is no fee for attendance.

Industrial Medicine in the Welfare State

A residential course on "The Role of Industrial Medicine in the Welfare State," arranged by the Nuffield Department of Occupational Health, will be held at Ashburne Hall, the University of Manchester, from Monday evening, March 27, to Saturday midday, April 1. The course is intended for industrial medical officers and industrial nursing sisters. The full programme may be obtained from the Secretary, Nuffield Department of Occupational Health, University of Manchester, Manchester, 13.

International Society of Haematology

A congress of the International Society of Haematology will be held at Cambridge on August 21–26. Sessions will be devoted to discussions on anaemias, leukaemias, blood coagulation, and immuno-haematology. The wives of delegates will be entertained by excursions and there will be social functions in the evenings. Anyone who wishes may attend or offer a paper, but since accommodation in Cambridge is limited they should apply at once to the Congress secretary-treasurer, Dr. Martin Hynes, Department of Medicine, University of Cambridge.

SOCIETIES AND LECTURES

Saturday

N.E. METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At Harts Sanatorium, February 4, 2.30 p.m., *"Art Therapy,"* by Dr. Duff Palmer; *"Bronchial Obstruction in Primary Pulmonary Tuberculosis,"* by Dr. W. F. Richards.

Monday

LONDON COUNTY MEDICAL SOCIETY.—At Fountain Hospital, Tooting Grove, London, S.W., February 6, 2.30 p.m., clinical meeting.

Tuesday

LONDON UNIVERSITY.—At Westminster Medical School (Meyerstein Lecture Theatre), Horseferry Road, London, S.W., February 7, 5 p.m., *"The Circulation in Disease,"* by Professor J. G. G. Borst (University of Amsterdam).

UNIVERSITY COLLEGE, Gower Street, London, W.C.—February 7, 5.15 p.m., *"Visual Physiology,"* by Dr. L. C. Thomson.

Wednesday

CAMBRIDGE UNIVERSITY.—At Addenbrooke's Hospital, Cambridge, February 8, 2.30 p.m., *"Medical Services in the U.S.A.,"* by Professor A. Leslie Banks.

EDINBURGH CLINICAL CLUB.—At Royal Hospital for Sick Children, Edinburgh, February 8, 4 p.m., clinical meeting, by Professor R. W. B. Ellis and Mr. J. J. Mason Brown.

INSTITUTE OF UROLOGY.—(1) At St. Peter's Hospital, Henrietta Street, Covent Garden, London, W.C., February 8, 3.30 p.m., Ward Round by Mr. H. Rees; (2) At St. Paul's Hospital, Endell Street, London, W.C., February 8, 5 p.m., *"Calculous Disease of Kidney and Ureter,"* by Mr. H. P. Winsbury-White.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242, St. Vincent Street, Glasgow.—February 8, 5 p.m., *"Recent Advances in the Diagnosis of Congenital Heart Disease,"* James Watson Prize Lecture by Dr. G. J. Aitken.

SOUTH WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, Wandsworth Common, London, S.W., February 8, 8.30 p.m., demonstration of clinical cases by medical staff.

Thursday

ADLERIAN SOCIETY OF GREAT BRITAIN: MEDICAL SECTION.—At 11, Chandos Street, London, W., February 9, 8 p.m., *"Psychotherapy and Responsibility,"* by Professor F. L. Golla.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—February 9, 5 p.m., *"Urticaria,"* by Dr. A. D. Porter.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., February 9, 5 p.m., *"Pathology of Calculous Disease,"* by Dr. C. Dukes.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—February 9, 5 p.m., *"Congenital Deformities of the Urethra, Vagina, and Anus,"* Hunterian Lecture by Professor Denis Browne.

ROYAL SANITARY INSTITUTE.—At Town Hall, Lancaster, February 9, 2 p.m., *"The Care and Treatment of the Elderly Sick and Infirm,"* by Alderman Mrs. M. M. C. Kemball; *"Recent Progress in the Methods of Hygiene as Applied to the Production of Milk and Ice Cream,"* by Harri Heap, M.Sc., F.R.I.C.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—February 9, 4.30 p.m., *"Psychiatry,"* lecture-demonstration by Dr. D. Curran.

TORQUAY AND DISTRICT MEDICAL SOCIETY.—At Torbay Hospital, February 9, 8.30 p.m., *"Modern Clinical Endocrinology,"* by Dr. S. L. Simpson.

Friday

MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, Maida Vale, London, W.—At Medical School, February 10, 5 p.m., neurological demonstration by Dr. Helen Dimsdale.

NATIONAL HOSPITAL, Queen Square, London, W.C.—February 10, 5 p.m., *"Occurrence of Neuropsychiatric Disorder in Twins,"* by Dr. Helgi Tomasson (Iceland).

ROYAL INSTITUTE OF PHILOSOPHY, University Hall, 14, Gordon Square, London, W.C.—February 10, 5.15 p.m., *"Morality: Tradition and Reason,"* by Mr. Karl Britton (University College of Swansea).

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—February 10, 8 p.m., dissertation by Mr. L. R. Roberts.

SOCIETY OF CHEMICAL INDUSTRY: FINE CHEMICALS GROUP.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C., February 10, 7 p.m., *"The Economics of the Fine Chemical Industry,"* by Mr. J. Davidson Pratt.

UNIVERSITY COLLEGE, Gower Street, London, W.C.—February 10, 5.15 p.m., *"Aspects of Pharmacological Chemistry,"* by Dr. F. Bergel.

WEST KENT MEDICO-CHIRURGICAL SOCIETY.—At Miller Hospital, Greenwich High Road, London, S.E., February 10, 8.30 p.m., *"The Discomforts of Pregnancy,"* by Mr. Alistair L. Gunn.

WHIPPS CROSS HOSPITAL MEDICAL SOCIETY, Whipps Cross Hospital, London, E.—February 10, 8.30 p.m., *"The Care of the Elderly,"* by Mr. L. Z. Cosin.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Brandon.—On January 19, 1950, at Rotunda Hospital, Dublin, to Joan (née Hallows), wife of Dr. Richard E. Brandon, of 9, Trimleston Avenue, Booterstown, Co. Dublin, a daughter.

Buchanan.—On January 21, 1950, at 11, Randolph Crescent, Edinburgh, to Hetty, wife of Dr. J. W. Buchanan, a daughter.

Cant.—On January 11, 1950, at Point Fortin Hospital, Trinidad, B.W.I., to Gillian (née Wrong), wife of Dr. F. E. V. Cant, a son—James Murray.

Goodman.—On January 10, 1950, to Ruth (née Sabel), M.B., Ch.B., D.R.C.O.G., wife of Cyril J. Goodman, 20, Dorset Square, London, N.W., a daughter—Sarah.

Lord.—On January 19, 1950, at Barton House, Stockton-on-Tees, to Dr. and Mrs. W. J. H. Lord (Reda Williamson), a daughter.

Tata.—On January 20, 1950, at Castlebar, Sandy Lane, Billingham, Co. Durham, to Monica (née Whelan) and Dr. M. N. Tata, a son, *Deo gratias*

DEATHS

Bond.—On January 14, 1950, at Huon, Ewell, Surrey, Charles Shaw Bond, M.B., B.Chir., D.P.H., aged 80.

Campbell.—On January 17, 1950, at 81, Blackness Avenue, Dundee, Henry Gordon Campbell, L.R.C.P.&S.Ed., L.R.F.P.S., L.D.S.

Falk.—On January 18, 1950, at 42, Heathhurst Road, Sanderstead, Surrey, Herman Falk, M.B., Ch.B., L.D.S., Major, I.M.S., Ret.

Hayman.—On January 13, 1950, at 39, South Drive, Queen's Park, Bournemouth William Speed Hayman, M.B., M.R.C.S., aged 91.

Hick.—On January 19, 1950, at 92, Kent Road, Swindon, Wilts, Rupert Bannatyne Hick, M.R.C.S., L.R.C.P., aged 60.

Hingston.—On January 16, 1950, at Datchet, Bucks, William Perceval Hingston, C.B., M.R.C.S., L.R.C.P., Surgeon Captain, R.N., Ret.

Hornibrook.—On January 20, 1950, at The Holt, Gerrards Cross, Bucks, William Henry Hornibrook, F.R.C.S.I., aged 81.

Lazarus-Barlow.—On January 15, 1950, at Bexhill-on-Sea, Sussex, Walter Sydney Lazarus-Barlow, M.D., F.R.C.P., aged 84.

McDiarmid.—On January 16, 1950, at Tighanalt, Fochabers, Morayshire, Patrick McDiarmid, M.B., Ch.B.

Morris.—On January 1, 1950, at Basil Grange, Sandfield Park, Liverpool, Thomas Glynn Morris, M.D., aged 80.

Mort.—On January 19, 1950, at Rock House, Worsley, near Manchester, James Henry Mort, M.R.C.S., L.R.C.P., J.P., aged 78.

Mudd.—On January 15, 1950, at 43, Pembroke Avenue, Worthing, Sussex, Barrington William Mudd, M.B., C.M., J.P.

Nelson.—On January 6, 1950, in a London hospital, Wallace Nelson, M.B., Ch.B., Colonial Medical Service, of Red Ridge, Banks Road, Sandbanks, Bournemouth.

Orchard.—On January 1, 1950, at the Hermitage, Kingussie, Inverness-shire, Edward Russell Orchard, M.B., C.M.

Patterson.—On January 16, 1950, at Nobs Crook, Ashridge Park, Herts, Norman Patterson, F.R.C.S.

Rankin.—On January 6, 1950, at Inverness, Donald Rankin, M.B., Ch.B., of Fort William, Inverness.

Ruxton.—On January 11, 1950, Mrs. Mabel Halden Ruxton (née Naylor), M.B., B.S., of 9, The Butts, Brentford, Middlesex.

Steele.—On January 8, 1950, at Deanfield, Londonderry, N. Ireland, William Caldwell Steele, M.B., C.M., late of Walthamstow, London, E.

Sweeney.—On January 16, 1950, at St. Mary's Hospital, London, W., Edward Reginald Stanislas Sweeney, M.R.C.S., L.R.C.P., of 34, Elgin Crescent, London, W.

Taylor.—On January 18, 1950, at Wareham, Dorset, Ernest Charles Taylor, M.B., Ch.B., Major, I.M.S., Ret., aged 74.

Toukhy.—On December 30, 1949, at Hurst Hill, Bilston, Staffs, Mahmoud Said Toukhy, M.B., Ch.B.

No. 2

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended January 14.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1950 (a)	1950 (b)	1950 (c)	1950 (d)	1950 (e)	1949 (Corresponding Week) (a)	1949 (b)	1949 (c)	1949 (d)	1949 (e)
Meningococcal infection	41	1	23	1	—	43	2	25	7	4
Deaths		1	—				—	1		
Diphtheria	81	8	18	5	2	126	9	41	8	5
Deaths	1	—	—	—	—	2	—	—	—	—
Dysentery	154	18	44	—	—	81	21	26	1	5
Deaths				—	—				—	—
Encephalitis, acute	5	1	1	—	—	—	—	—	—	—
Deaths		—					—			
Erysipelas			29	12	5			28	9	4
Deaths							—			
Infective enteritis or diarrhoea under 2 years				20	7				39	
Deaths	26		5	2	3	54	5	5	2	6
Measles*	2,318	54	48	87	218	13,185	318	61	55	143
Deaths†			—	—	—			—	1	—
Ophthalmia neonatorum	27	2	7	—	—	50	5	5	2	1
Deaths										
Paratyphoid fever	—	—	—	—	—	2	—	—	—	—
Deaths	—		—	—	—	1	—	—	—	—
Pneumonia, influenzal	991	79	22	7	7	1,181	55	18	8	9
Deaths (from influenza)‡	47	8	6	2	—	47	6	5	2	—
Pneumonia, primary			439	¶				447	48	
Deaths	300	49		13	11	435	75		8	13
Poliomyelitis, acute	50	5	1	4	—	20	2	2	—	—
Deaths§	9	—				2	—			
Puerperal fever		—	10		—		—	9		—
Deaths										
Puerperal pyrexia‖	70	6	9	1	2	73	3	4	1	—
Deaths							—			
Relapsing fever	—	—			—	—	—			2
Deaths										
Scarlet fever	1,758	92	261	62	162	1,022	53	230	113	40
Deaths†			—	—	—			1	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	8	—	1	—	—	4	—	—	—	—
Deaths	1	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	1,535	59	359	50	67	2,306	168	141	63	39
Deaths	4	—	—	—	—	12	—	2	1	1
Deaths (0–1 year)	294	40	43	25	15	424	50	68	31	24
Deaths (excluding stillbirths)	5,520	916	652	225	138	6,698	999	988	256	195
Annual death rate (per 1,000 persons living)			13.1					19·9	15·9	
Live births	7,201	1142	915	385	229	8,066	1314	1061	444	243
Annual rate per 1,000 persons living			18·4					21·4	27·5	
Stillbirths	191	23	22			207	35	25		
Rate per 1,000 total births (including stillborn)			23					23		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

¶ Primary pneumonia no longer notifiable in Eire.

EPIDEMIOLOGICAL NOTES

Typhoid Fever in Walthamstow Area

Six cases of typhoid fever in Walthamstow and the neighbouring districts in North-east London have been traced to a carrier working in a café frequented by workers in local factories and by casual callers engaged in transport. The carrier has been suspended from work. The onset of illness in notified cases was in the latter half of December and the first week of January. The organism is of Vi-phage type E1.

Discussion of Table

In *England and Wales* there were decreases in the notifications of acute pneumonia 129, dysentery 45, scarlet fever 40, and typhoid fever 20, while the only increased incidence of any size was 156 for whooping-cough.

Notifications of scarlet fever decreased in Yorkshire West Riding 35 and London 30, and increased in Durham 27. Slightly over one-half of the notifications of measles were contributed by three counties: Lancashire 445, Durham 404, and Norfolk 345. The chief variations in the incidence of measles were increases in Durham 73 and Lancashire 57, with decreases in Suffolk 30 and Norfolk 25.

The chief feature of the returns for whooping-cough was an increase of 69 in the notifications in Lancashire. A decrease of 9 was recorded in the number of notifications of diphtheria in Lancashire. In most parts of the country there was a small decrease in the incidence of acute pneumonia.

Only 3 cases of dysentery were reported from Staffordshire, Smethwick C.B., where 86 cases were notified in the preceding week. The largest returns of dysentery were Lancashire 26 (Liverpool C.B. 9); Yorkshire West Riding 25 (Leeds C.B. 14); London 18; Durham 15; Northumberland 14 (Newcastle-upon-Tyne C.B. 13); Sussex 10 (Horsham R.D. 10).

In *Scotland* there were increases in the notifications of whooping-cough 212, measles 36, and acute primary pneumonia 31, with a decrease of 10 in the incidence of dysentery. The rise in the notifications of whooping-cough was general throughout the country and is probably mainly due to the new regulation making whooping-cough compulsorily notifiable rather than to a large increase in actual incidence. The chief returns for dysentery were Glasgow 29, Edinburgh 6, and Ayr county 6.

In *Eire* there was a decrease of 27 in the notifications of scarlet fever. This fall was mainly due to the experience of Dublin C.B.

In *Northern Ireland* a decrease of 16 in the notifications of scarlet fever and an increase of 17 for whooping-cough were the only variations in the general trends of infectious diseases. There was, however, considerable variation in the local returns of measles, the largest being falls in Antrim county 32 and in Down county 22, and increases in Belfast C.B. 15 and Londonderry county 20. A fall of 22 in the notifications of scarlet fever was reported from Belfast C.B.

Week Ending January 21

Notifications of infectious diseases in England and Wales during the week included: scarlet fever 2,023, whooping-cough 1,753, diphtheria 74, measles 2,334, acute pneumonia 890, acute poliomyelitis 51, dysentery 177, paratyphoid fever 1, typhoid fever 5. Deaths from influenza in the great towns numbered 39.

A circular from the Ministry of Health to hospital boards and committees emphasizes the importance of sterilizing hospital kitchen-waste (swill). Users of swill are statutorily required to see that no farm livestock come into contact with raw swill, and to boil the material for one hour before feeding it to stock. This is only a minimum precaution, and sterilizing plants have been set up in most populous areas to provide better sterilization. Where these plants are available local authorities collect the kitchen waste and send it to them.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Hernia and Injury

Q.—*Is there any relation between injury and inguinal hernia, both direct and indirect, in the adult? To what extent is it correct to attribute hernia to single or repeated strains, or to assume that a hernia already present can be aggravated by trauma?*

A.—Inguinal hernia is due to two causes: an actual or potential weakness in the musculature of the anterior abdominal wall and an increase of intra-abdominal pressure. In respect of the first factor injury can have effect only through the weakening and stretching of a scar—surgical or otherwise. Reflex contraction of muscles due to actual injury, or in anticipation of injury, can certainly increase intra-abdominal pressure to the extent of pushing out either a direct or an indirect inguinal hernia—the former more frequently and the latter when there is a pre-formed sac. The more fat the patient and the more atonic his abdominal musculature, the more likely this is.

It is certainly true that either a sudden single strain or repeated strains (producing a rise of intra-abdominal pressure) can aggravate an existing hernia. It is well known that, where a bilateral inguinal weakness exists, satisfactory surgical repair of one side is often sufficient to produce an actual herniation of the (weak) opposite side. Where the proof of sudden or recurrent strain is sufficient, all herniae acquired during military service are pensionable.

Antihistamines and Histamine Desensitization

Q.—*Antihistamine drugs are successfully used in the treatment of hay fever and other atopic conditions. Can a similar but more lasting effect in such conditions be expected by desensitizing the individual with subcutaneous injections of histamine?*

A.—There does not appear to be any correlation between the results obtained with antihistamine drugs and those following histamine desensitization. Histamine desensitization has been used quite extensively in the past in cases of urticaria, but the results were disappointing, and this form of therapy has now been given up almost completely. The antihistamine drugs are, of course, very helpful in the treatment of urticaria. Histamine therapy has been tried in other atopic conditions to a lesser extent, but with no striking success.

Sex Hormones and Bone Growth

Q.—*Has testosterone any action on the rate of callus formation? What is the optimum dosage and preparation, if it is of benefit? Have the oestrogens any similar effect on bone growth?*

A.—This is not an easy question to answer. In mice both testosterone and oestradiol inhibit the proliferation of the cartilage and accelerate skeletal ageing. This does not appear to be true in man, at least not for therapeutic doses of these hormones. If, however, hypogonadism with or without adiposity is associated with a slipped epiphysis of the upper end of the femur in children, testosterone under these particular circumstances will often produce union of the epiphysis and shaft in both sexes—a valuable therapeutic effect. In rats, both testosterone and oestradiol increase the phosphatase content of the femur. Oestrogens cause the deposition of calcium in bones in mice, and bring about a rise in the blood calcium in birds and fishes. In man, testosterone was reported as producing a rise in serum calcium in patients with carcinoma of the breast and bony metastases, but this report has not been confirmed by subsequent workers who have found no such change. However, testosterone does seem to diminish pain and produce recalcification of osseous metastases, and it may effect union of a pathological fracture in such cases. The rarefaction of bones in older people is thought to be associated with a decreased secretion of oestrogens and androgens.

As to dosage, the usual dosage for replacement therapy in androgen deficiency is 25 mg. of testosterone propionate intramuscularly daily, but four times this dose has been used in cases of carcinoma of the breast with metastases. The disadvantages in the female are the development of acne, hirsutism, and plethora when large doses are used over a long period. For children 5 mg. methyl testosterone by mouth three times daily may be adequate.

Offspring of a Mixed Marriage

Q.—*An English girl is very anxious to marry a man whose grandmother on his father's side was Indian, the rest of his forebears being English or Scots. If this union were to come about, can any reasonable forecast be made whether (a) the children would be likely to be very obvious Eurasians, and (b) if one or more of the children would show very marked Asiatic characteristics? The man himself does not possess many Asiatic characteristics.*

A.—The most that can be said in broad general terms on the basis of the information given is that the children of such a marriage would tend on the average to be intermediate between the father and the "normal English" type represented by the mother. In certain individual characteristics the paternal Eurasian traits might reappear, but it is unlikely that a child would look as Eurasian as the father and extremely improbable that any child would look more so.

Grafenberg Ring

Q.—*Why is the Grafenberg ring apparently widely used in the U.S.A. and so little used here? Statistics are said to show it to be highly effective, and a recent publication suggests that accidents associated with its use are unlikely.*

A.—The data forming the basis of this question require critical study. Is the Grafenberg ring being widely used in America, and, if so, by whom? There appears to be no evidence to show that practitioners of repute are being converted to its use and are finding it relatively innocuous. Even in this country, where the Grafenberg ring is seldom inserted, cases of injury, infection, menorrhagia, etc., all attributable to it, fall within the experience of nearly all gynaecologists. Nor is it so reliable in inducing abortion—for that is its action—as the question implies. The warning against its use published by the Family Planning Association in the *Journal* of October 19, 1946 (p. 599), still holds good.

Vaccination and General Immunity

Q.—*I have made fairly extensive inquiries among my friends and acquaintances and have reached a very definite conclusion that children who have been vaccinated are much more susceptible to the other zymotic diseases than those to whom this protection has not been given. Has this point ever been raised before, and is there any evidence on it?*

A.—A satisfactory answer to this question could be obtained only by taking a large number of babies picked at random, dividing them, again by random sampling, into two groups, vaccinating one group, and then following up all the babies for four to five years during the time when they might be expected to develop the common childhood fevers. Individual impressions about whether vaccinated babies fare better or worse than unvaccinated babies must be unreliable for a number of reasons—for example, the vaccinated babies are a selected group, since there was a variety of excuses in the "compulsory era" which could be put forward for not having the child vaccinated; in fact, only about 30% of the infant population was vaccinated in the years before July, 1948. Parents and doctors may be biased either in favour of or against vaccination, and therefore inclined to attribute good or ill after-effects to

vaccination. Thus, one fairly careful follow-up early in this century (but not a properly controlled investigation as we now understand it) showed that vaccinated babies suffered less from other infectious diseases than did the unvaccinated; but, since sickly babies and perhaps also the offspring of the less intelligent and poorer parents were likely to be included in the unvaccinated group, a bias was immediately introduced. There is no theoretical reason why the vaccinated infant should suffer more from infectious diseases than the unvaccinated; indeed, if vaccination in infancy helps to stimulate the development of the antibody-producing cells, the child might thereby be better able to resist other infections.

Urinary Incontinence

Q.—*Is there any apparatus suitable for a middle-aged man who has remained incontinent after the removal of a carcinoma of the prostate? He wears a leg urinal during the day, but at night he is unable to arrange any method of keeping the bed dry.*

A.—Rubber urinals for urinary incontinence are often very unsatisfactory at night. The continuous use of them is also liable to produce irritation and soreness of the glans penis. Many patients learn to sleep on their backs and to keep the bed dry by maintaining the usual wide-mouthed bottle between their thighs. If this is not possible and the bladder has a reasonable capacity, the continuous escape of urine from the urethra can sometimes be prevented by wearing a light adjustable penile clip. This means, of course, that from time to time the patient is awakened by an urgent desire to pass water, and must then remove the clip. Should these methods fail, the only thing left to do is to place some highly absorbent material on the rubber sheet, and for this purpose pads of sphagnum moss, such as were used in the first world war when patients suffering from heavily discharging wounds had to make long journeys without any chance of their dressings being changed, should be employed.

Food Allergy

Q.—*Is it possible to desensitize a patient who has had asthma since the age of four and has always been allergic to fish and eggs? By avoiding fish and eggs she was completely free from asthma while at school, but she is now having occasional attacks after eating, for example, cakes which she did not know contained eggs.*

A.—Desensitization in the strict sense is not possible and the value of hyposensitization to foods is questionable. The comparatively satisfactory results of pollen hyposensitization, introduced by Noon and Freeman almost forty years ago and now universally accepted, naturally led to the hope that similar satisfactory results might be obtained in cases of food allergy. Unfortunately, but very strikingly, published results show that consistently favourable results have not been obtained and that this method of treatment has been almost completely given up at the present time. Even where apparently satisfactory results were obtained it was difficult to be certain that the results were due to the hyposensitization, for it is known that 90% to 95% of children outgrow their food allergies. Hyposensitization should not be undertaken in fish-sensitive cases, nor when the sensitivity is very marked, as it is here to eggs, which even in cakes produce asthma, owing to the danger of a severe constitutional reaction.

Colostomy and Pregnancy

Q.—*I have a patient, aged 23, who has a sacral colostomy to circumvent an imperforate anus. She is about to be married. Would pregnancy be liable to upset her colostomy, and what are the chances of the anal defect being passed on to her children? Her genital organs appear to be normal.*

A.—Pregnancy and labour should not raise any special problem in this case, although, as always, a tendency to constipation and some difficulty in ensuring regular bowel action is to be expected. Genetic factors probably play some part in the aetiology of imperforate anus, but it does not show such a strong familial tendency as do some other malformations. The risk of offspring being affected is probably very small, especially if none of the other relatives and antecedents of the woman have suffered congenital malformations and if the prospective husband is of untainted stock.

Repeated Injection of Tetanus Antitoxin

Q.—(*a*) *When is the injection of tetanus antitoxin after an injury contraindicated?* (*b*) *Would it be safe to administer it routinely on several occasions to the same individual?*

A.—(*a*) The injection of a foreign protein such as tetanus antitoxin is contraindicated, without previous sensitivity tests, in any individual with an allergic history—e.g., a recent or past sufferer from asthma, hay-fever, eczema, or urticaria—since an injection of a foreign protein may induce an acute anaphylactic reaction with death in 10 to 30 minutes. Fortunately this form of anaphylaxis is extremely rare in man.

(*b*) Tetanus antitoxin may be given repeatedly at intervals of one week or less without risk of reaction; this procedure was recommended and often used for severe war wounds and air-raid casualties during the recent war. The main danger from the repeat injection lies in the interval of time between the inoculations. If it exceeds ten days the patient's tissues become sensitized and often react violently to the second injection, with substernal pain and oedema of the tissues, which in the glottis may cause acute respiratory obstruction. With an increasing interval of time, and depending to some extent on the size of the initial dose, the risk of this type of reaction from the second injection steadily diminishes, but any person giving a history of having had antiserum within recent years should first be tested for sensitivity by intradermal injection of diluted antitoxin, and, if need be, desensitized before any additional antiserum is given.

NOTES AND COMMENTS

Salicyl-sulphonic Acid Test.—Dr. JAMES KAY (St. Helens, Lancs) writes: I would like to support the observation of Dr. A. Michael Davies (December 31, 1949, p. 1540) that the salicyl-sulphonic acid test is more delicate than the heat test in detecting the presence of protein in the urine. It is the delicacy and simplicity of this cold test which appeal, especially to those examining large numbers of specimens of urine. In an antenatal clinic I made it a routine to test all very weakly positive salicyl-sulphonic acid tests with the heat test, and not invariably the latter was negative. With experience one can learn to ignore the very weakly positive test.

Corrections

Since publication of the leading article "Shortage of Rh Testing Sera" (January 14, p. 108) we have been informed by Armour and Co., Ltd., that they believe supplies of bovine albumin to have been ample since 1946, and the statement in the leading article, "The latter substance [bovine albumin] is available in England only in very small quantities," may thus have given a misleading impression.

Mrs. T. B. JOBSON (Guildford) writes: I have just been reading the obituary notice of Dr. Justina Wilson (January 14, p. 132). I feel I must point out an error. It is stated that Dr. Justina Wilson "opened a school, 'the Swedish Institute,' in Cromwell Road." This is incorrect, as the Swedish Institute was opened by Dr. Mary Coghill-Hawkes in 1904. I was one of her many students and was also a student for a short time under Dr. Justina Wilson when Dr. Coghill-Hawkes sold her school to Dr. Wilson in 1917. As Dr. Mary Coghill-Hawkes was a pioneer of schools of this type I think that she should receive the credit.

In previous notices in the *Supplement* of B.M.A. scholarships in aid of scientific research the last date for the receipt of applications was given as April 28, 1950. This should have read Friday, March 31, 1950, as shown at p. 50 of the *Supplement* this week.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone. Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.
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